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RELIEF OF PAIN BY MESENCEPHALIC TRACTOTOMY

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The convergence of the spinothalamic and the secondary trigeminal tracts in the pons makes it possible to section the pain pathways from one half of the body without appreciably damaging other nerve structures. This may be accomplished in the upper part of the pons or the mesencephalon. Dogliotti,[1] who first suggested section of these pathways in the brain stem, made his incision in the rostral portion of the pons. Because of the easier surgical approach and the clearer surface markings of the pain tracts in the mesencephalon, this level seems more favorable for the section (fig. 1). Two cases in which this procedure was carried out have been previously published.[2] Three additional cases are reported here.

REPORT OF CASES

CASE 1.—A. S., a 26 year old bartender, was admitted to the University of Chicago Clinics, service of Dr. Charles Huggins, on April 1, 1940. Three to four months before entrance, after a mild trauma, he noticed a swelling of the left testicle. The swelling continued for about two months and then remained stationary. During that time the patient had slight pain in the nipples, but the breasts did not alter in appearance. Except for a loss of weight of 5 to 8 pounds (2.3 to 3.6 Kg.), inquiry concerning function revealed no other relevant information. The past, family and personal histories did not yield any contributory data.

Physical examination was not significant except for the local findings. The right testicle was smaller and softer than normal. The left scrotum was distended by a firm mass, the size of an apple, replacing the testicle. The superior pole of this mass was soft and fluctuant; the remainder was firm and resilient and was opaque on transillumination. The left spermatic cord was thickened to the size of a thumb.

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Read before the Section on Nervous and Mental Diseases at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Dogliotti, M.: First Surgical Sections, in Man, of the Lemniscus Lateralis (Pain-Temperature Path) at the Brain Stem, for the Treatment of Diffuse Rebellious Pain, Anesth. & Analg. **17**:143-145 (May-June) 1938.

2. Walker, A. E.: Mesencephalic Tractotomy: A Method for the Relief of Unilateral Intractable Pain, Arch. Surg. **44**:953-962 (May) 1942.

Rectal examination disclosed no abnormalities, and there was no evidence of pulmonary lesions in roentgenograms of the chest.

On April 10, Dr. C. M. Vermeulen performed a left orchiectomy, with the patient under spinal anesthesia. Histologic examination of the tumor, which weighed 197 Gm., showed it to be a teratoma of the testis.

Except for mild pains in the left flank, the patient had no further difficulty until November 1940, when the pain became almost unbearable. At that time a mass was palpated in the left upper quadrant. At approximately two month intervals three courses of roentgen therapy were given to the retroperitoneal glands. Three months later the patient returned because he was unable to obtain relief from his pain with morphine sulfate, 1 grain (0.065 Gm.) every four hours. In the meantime the pain had extended to the right side of the pelvis and into the lower ribs on the left side. Lying down so aggravated the pain that he slept in the sitting position.

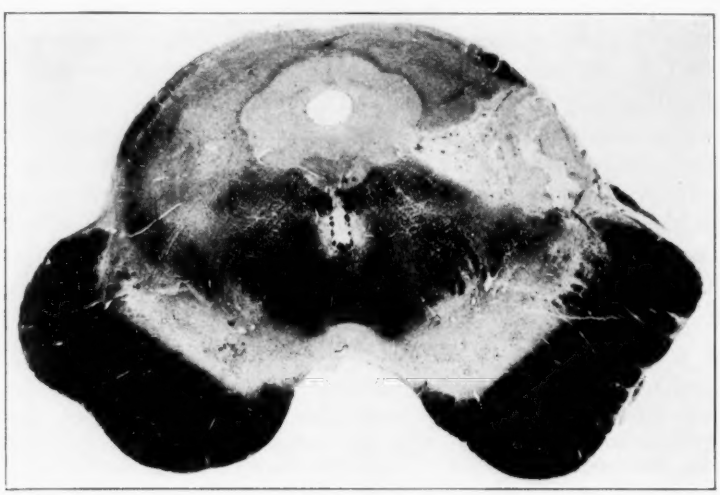

Fig. 1.—Photomicrograph of the mesencephalon, showing the location of the tractotomy.

The patient was severely emaciated and obviously in great pain. There was an irregular-shaped, firm, nontender mass, 3 by 3 by 4 cm., under the left sternocleidomastoid muscle just above its insertion. The head and neck were otherwise normal. There were firm inguinal nodes on both sides. The left testis was absent; the right was normal.

Neurologic examination disclosed nothing pathologic except that the left leg was weaker and warmer than the right. There was tenderness on percussion of the lower lumbar vertebrae. On lifting the head the umbilicus was drawn cephalad 1 cm. (positive Beevor's sign). Roentgenograms of the chest and pelvis were negative for evidence of metastases.

Because of the patient's desire to avoid impotence, it was planned to do a mesencephalic tractotomy on the right side and later a left unilateral chordotomy.

On Sept. 11, 1941 the patient was anesthetized with avertin with amylene hydrate and the line of the proposed incision infiltrated with 1 per cent procaine hydrochloride. A small bone flap was turned down in the right temporo-occipital region, the line of fracture being just above the lateral sinus. The dura was then

incised and reflected inferiorly. Several vessels passing to the lateral sinus were coagulated and clipped. On retracting the brain from the tentorium, more veins passing into the superior surface of the tentorium were coagulated and cut. The tentorium was then split to the incisura, a small ooze from the margin being controlled with silver clips. The arachnoid over the lateral surface of the mesencephalon was incised, which allowed the fluid from the cisterna ambiens to escape. The superior cerebellar artery, the trochlear nerve, the pes pedunculi and the brachium of the inferior colliculus were identified. A knife was then inserted into the lateral sulcus and carried superiorly across the brachium of the inferior colliculus. Only slight oozing occurred. The dura mater was tightly closed and the bone flap replaced, the skin being closed with two layers of black silk.

The patient awoke four hours after the completion of the operation and moved all four extremities. About eight hours later he withdrew from pinprick on the right side of the body but did not respond to it on the left side.

On the first postoperative day the patient was rational and cooperative. To confrontation tests there was left homonymous hemianopia. External ocular movements were full. The left corneal reflex was diminished as compared with the right. There was complete analgesia over the body, face and extremities on the left side. Finger to nose tests were well performed on both sides. The fingers were correctly identified, and position and vibratory sensibilities were intact. The heel to knee test was rather unsteadily performed on the left side. The patient voided normally.

On the third postoperative day the patient complained of pain only on the right side. The left arm and leg were said to be numb and to "feel funny." The visual fields were widening, although they were still constricted on the left side. There was no facial weakness. Hearing was grossly normal. Pinprick on the left side caused a peculiar, rather unpleasant tickling sensation. Rapidly alternating movements were well performed on the two sides. Hot and cold stimuli could not be differentiated on the left side.

The visual fields were full on the fourth postoperative day. Audiometer tests showed slight high tone deafness on the left side, but normal hearing on the right. The patient said that everything, even a cigaret, had tasted flat since the operation. Examination, however, did not disclose gross impairment of the appreciation of salt, sugar or quinine.

On the sixth postoperative day the hemianalgesia and hemithermanesthesia on the left side remained as previously. Pinprick on the left side produced a disagreeable sensation of tickling. There was one small area over the dorsum of the left foot where occasionally pinprick appeared to be appreciated as painful, and where occasionally heat and cold were appreciated as such. Pinprick was not felt well on either side of the tongue. On the eighth postoperative day the patient was up in a chair. The left hemianalgesia and hemithermanesthesia remained as previously. By the fourteenth postoperative day he was able to walk. Cinemas were taken at this time. Examination of the visual fields revealed slight left peripheral homonymous constriction. Audiometer tests were repeated; the impaired appreciation of high tones in the left ear was still present (fig. 2). The neurologic findings were much as before. Tactile sensibility had been tested over the previous three days with von Frey hairs. A 0.5 Gm. per millimeter hair was appreciated consistently on the right side of the cornea of both eyes but was said to be less acute on the left. The number of tactile stimuli appreciated in forty-nine trials is given in table 1.

Cutaneous temperatures were practically the same at comparable points on the two sides, except in the legs, and almost identical with the cutaneous temperature readings made before operation. The left foot was still considerably warmer than the right (preoperative temperature 35.6 and 32.5 C. [94 and 90 F.]; postoperative temperature 35.0 and 31.2 C. [95 and 88 F.]).

It had been decided to perform the chordotomy on the sixteenth postoperative day, but the previous day the patient complained of increasing weakness of the left leg. On the morning of the sixteenth day complete sensory and motor paralysis developed below the tenth dorsal dermatome. The patient slowly became weaker and died sixty-eight days after operation. There was little change in the neurologic status after the third week. The left hemianalgesia and hemithermanesthesia persisted, although at times he appeared to have a slight appreciation of pain over the left side of the forehead. Pinprick produced a disagreeable diffuse tickling sensation, which the patient insisted was not pain but which was even more unpleasant and intolerable than pinprick on the other side. On one occasion deep breathing

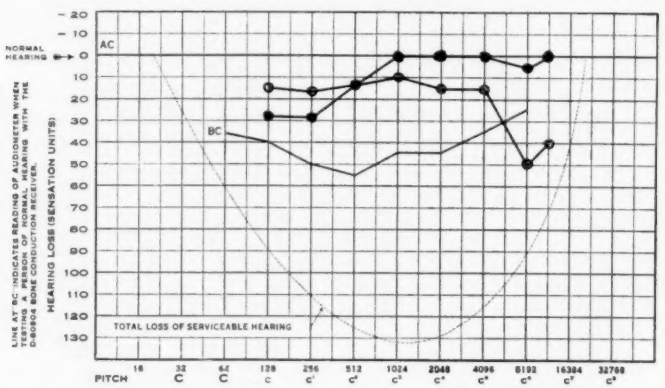

Fig. 2. (case 1).—Audiograms taken two weeks after mesencephalic tractotomy. The audiogram for the right ear is represented by large dots; that for the left, by circles.

TABLE 1.—*Number of Tactile Stimuli (Von Frey Hairs) Appreciated in Forty-Nine Trials*

Hair	Forehead		Cheek		Hand (Dorsum)		Foot (Dorsum)	
	Right	Left	Right	Left	Right	Left	Right	Left
0.5 mg./mm.	13	3	46	10	0	0	..	..
1.0 mg./mm.	15	0	46	8	5	0	..	..
2.0 Gm./mm.	42	2	49	36	7	..	..	..
3.0 Gm./mm.	..	..	..	..	8	..	..	..
4.0 Gm./mm.	49	12	..	..	..	..	..	..
5.0 Gm./mm.	..	..	49	48	7	8	5	0
10.0 Gm./mm.	..	..	49	49	6	4	14	0
15.0 Gm./mm.	..	..	..	..	30	6	16	4
20.0 Gm./mm.	..	..	..	..	45	7	40	6

caused pain in the left side of the chest. Examination of the abdomen by deep palpation caused no pain on the left side but produced distress on the right. No pain was elicited on strong compression of the bones of the left hand and forearm.

Pinching the left ulnar nerve caused a "funny" feeling (not pain) with radiation to the chest. Heat and cold could not be distinguished on the left side, the ice cold tube usually being called warm.

Unfortunately, permission for an autopsy could not be obtained. It is, therefore, impossible to make an accurate analysis of this case. The patient obtained complete relief from pain on the left side of the body after the operation. There was not, however, absolute analgesia on this side. The perception of pinprick was abnormal; in fact, there appeared to be a certain hyperpathia. The paraplegia which developed two weeks after operation was probably the result of epidural metastases, and was unrelated to the operative procedure.

CASE 2.—F. B., a man aged 67, was referred to the neurosurgical service on Jan. 25, 1942 because of severe, intractable pain, mainly confined to the left side of the face. In July 1939, after severe gingivitis, his right upper incisor teeth were removed. Biopsy of tissue from the upper alveolar ridge led to the diagnosis of osteogenic sarcoma. At a second biopsy in December 1939 the diagnosis of fibrosarcoma was made. In March 1940 the right upper alveolar ridge and part of the bony floor of the nose were removed surgically. The soreness persisted and became so severe that morphine was required. Injections of alcohol in the infraorbital nerve were unsuccessful. A tumor mass then appeared on the left upper alveolar ridge, which biopsy revealed to be fibrosarcoma.

On June 26, 1941 Dr. A. Brunschwig removed a large part of the left maxilla, leaving a gaping defect in the upper lip. This deformity was repaired in six stages by a pedicle skin graft.

In the latter part of October 1941 the pain returned, accompanied by a firm swelling of the hard palate. In two stages (October 31 and November 28) the tumor was removed, but incompletely, because of involvement of the entire hard palate and right axilla. Because of the severe, intractable pain the patient was readmitted on Jan. 25, 1942. The pain was most severe in the left maxillary region at the side of the nose. This area was tender to touch and pressure.

Physical examination showed no abnormality except about the maxillas. The left maxilla and the left side of the hard palate were missing, leaving a gaping defect in the roof of the mouth and the upper lip. The latter was partially repaired by a pedicle skin graft, but even with this the lips could not be approximated. Speech was accordingly nasal, husky and difficult to understand. Neurologic examination revealed no abnormalities. Attempts to determine threshold values for pain and tactile stimuli on the face and hands with von Frey hairs were unsuccessful, owing to lack of cooperation.

Examinations of the blood had shown mild secondary anemia, which was still present at the time of this admission. The hemoglobin content was 12.5 Gm. per hundred cubic centimeters, and the blood contained 4,300,000 red cells per cubic millimeter.

On January 27 the patient was anesthetized with avertin (90 mg. per kilogram) with amylene hydrate. The skin of the proposed incision was infiltrated with 1 per cent procaine hydrochloride. A small osteoplastic flap was turned down in the right occipital region, the posterior neck muscles being used as a hinge. The dura was reflected inferiorly. Vessels passing into the lateral sinus were coagulated and cut. The occipital lobe was then elevated and the tentorium incised to the incisura. The arachnoid about the lateral surface of the mesencephalon was teased away, exposing the cerebral peduncle, the fourth cranial nerve and several large veins lying on the cerebral peduncle. The lateral sulcus and the brachium of the inferior colliculus were readily identified. An incision 5 mm. deep was made from the

lateral sulcus superiorly to a point slightly more than halfway across the brachium of the inferior colliculus. The occipital lobe was allowed to fall back into place and the dura closed. The bone flap was replaced and the scalp closed with two layers of black silk.

The patient awoke late the day of operation but was too drowsy to be examined. The following day he was stuporous, restless and uncooperative. He voided in bed. The left side of the face appeared to be analgesic. He continued for several days in a semirational state, making examination difficult. There was, however, no weakness of the arms or legs. The extraocular movements were full. The

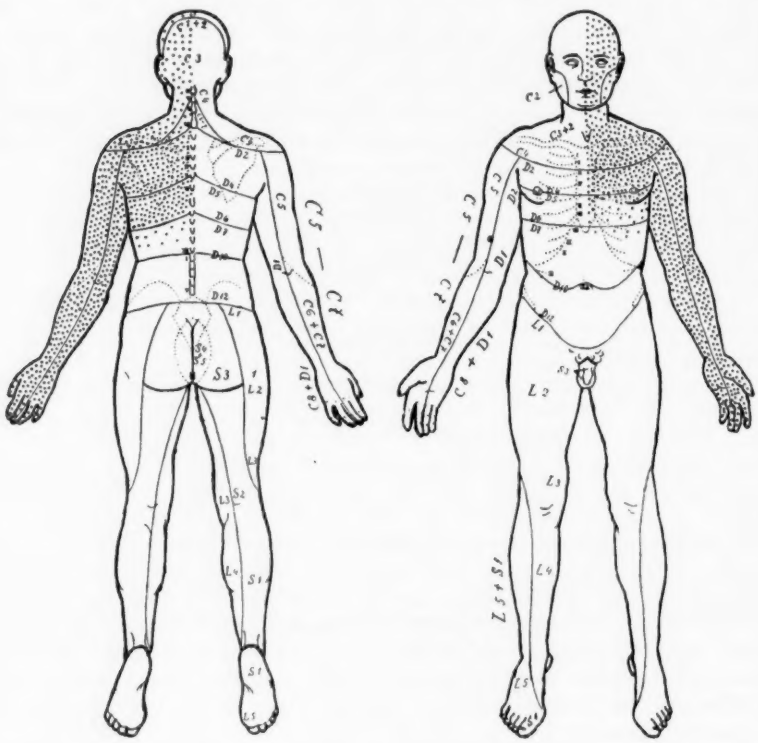

Fig. 3 (case 2).—Chart showing the sensory disturbances immediately after operation. Dense stippling represents analgesia and thermanesthesia; sparse stippling, hypalgesia and hypothermesthesia.

deep reflexes were normal throughout. There appeared to be analgesia over the left arm, extending to the nipple line, and hypalgesia over the face (fig. 3).

On the fourth postoperative day he had a sudden rise in temperature to 104.2 F. and was drowsy. Urinalysis showed albumin and 5 to 10 red blood cells per high power field. A lumbar puncture was performed. The initial pressure was 125 mm. of spinal fluid. The fluid was slightly xanthochromic and contained 160 cells, about 75 per cent of which were polymorphonuclear leukocytes. His temperature remained at this level for forty-eight hours and then gradually fell to normal limits.

On the sixth postoperative day he began to hiccup and vomited coffee grounds material. His abdomen became distended. Wangensteen gastric drainage relieved

the distress. The nonprotein nitrogen of the blood measured 40.6 mg. per hundred cubic centimeters. Neurologic examination on the eighth postoperative day revealed that the patient was drowsy and cooperated poorly, but was in no distress. The left corneal reflex was reduced as compared with the right. Pinprick was not appreciated as well on the left side of the face as on the right, but it was recog-

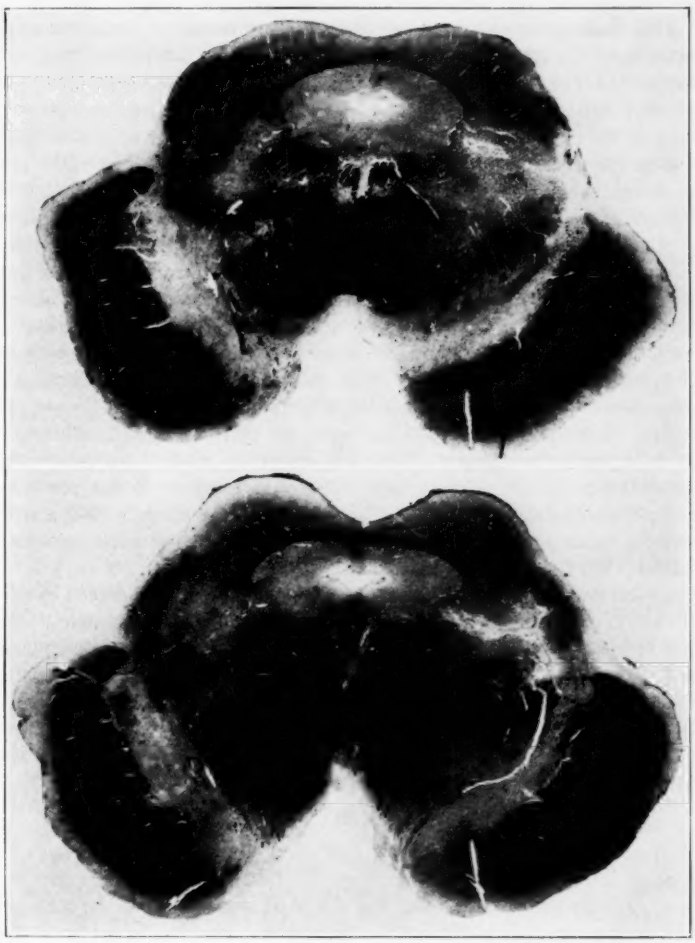

Fig. 4 (case 2).—Two sections of the mesencephalon, showing the greatest extent of the lesion. × 3.

nized as sharp. All movements of the extremities were possible but weak. The finger to nose test was well performed on both sides.

Cotton appeared to be appreciated well in all parts of the body. Vibratory and position senses were normal. Appreciation of pinprick was reduced over the left arm and the left side of the thorax. The tendon reflexes were active and equal on the two sides. Both plantar reflexes were flexor.

The patient's temperature gradually decreased, but the nonprotein nitrogen of the blood gradually increased, reaching 121.2 mg. per hundred cubic centimeters on March 2. His stupor decreased, and he became rational. Hiccup persisted but was fairly well relieved by morphine. On March 6 auricular fibrillation developed. During this period he had not complained of pain, although when questioned he stated that the left side of the face was still sensitive. Hypalgesia could still be demonstrated on the left side of the face, the left arm and the left side of the thorax. His hearing appeared grossly normal, but, owing to lack of cooperation, audiometer readings could not be made.

On March 17 he died suddenly. Complete postmortem examination (Dr. P. Steiner) revealed aspiration bronchopneumonia and sarcomatous metastases in the lower lobe of the right lung, acute hemorrhagic cystitis with diverticulosis, advanced fatty degeneration of the kidneys, thrombosis of a branch of the right posterior cerebral artery, with cerebral softening, and the site of a mesencephalic tractotomy.

The brain grossly appeared normal except for an area of softening on the lateral surface of the right occipital lobe, which measured 2.8 by 5 cm. It was lined by brownish, shaggy material, and its base appeared to communicate with the posterior horn of the ventricle. The site of the mesencephalic tractotomy was indicated by a small brownish discoloration lying on the lateral side of the mesencephalon, extending from the lateral sulcus to the middle of the brachium of the inferior colliculus.

Serial sections were cut of the brain stem. Every twenty-fifth section was stained by Nissl's technic and the adjacent section by the Smith-Quigley method for myelin. The lesion (fig. 4) was seen to extend from the lateral sulcus medially for 3 mm., damaging the lateral fibers of the medial lemniscus. A small lesion extended tonguelike dorsally and medially to reach the lower portion of the mesencephalic root of the fifth nerve. The lesion extended dorsally to approximately the middle of the brachium of the inferior colliculus, a considerable number of the fibers of the lateral lemniscus thus being spared.

The clinical course following operation in this case is well explained by the postmortem observations. The mental confusion, stupor and fever immediately following operation resulted from the cerebral softening precipitated by the manipulation of the brain. The renal failure and infection of the bladder accounted for the later symptoms.

Although the partial tractotomy appeared to give relief from pain, complete analgesia was not present after the first two weeks. Owing to the lack of cooperation, it was impossible to determine the degree of hypalgesia.

CASE 3.—G. A., a 41 year old meat packer, was referred by Dr. W. H. Lipman to the University of Chicago Clinics on Feb. 18, 1942, with the complaint of severe burning pains in his right, or fantom, hand. In November 1920 he caught his right hand in a sausage grinder, so mangling his arm that it had to be amputated at the upper third of the humerus. In 1933 he noticed a burning sensation in the hand of the fantom limb, which gradually increased in severity. Removal of neuromas from the stump gave relief for about six years. In 1940 the pain became severe again, and more neuromas were amputated. This procedure gave temporary and incomplete relief. On Aug. 28, 1941 a posterior cervical rhizotomy was performed, but the patient had as much, if not more, pain than previously. In December 1941 alcohol was injected into the stump, producing severe swelling but giving no relief. The pain was so severe that he could not sleep or work. At the time of admission he suffered three types of pain: burning sensation in the fantom hand, painful throbbing in the fantom hand and stump and a cramplike sensation in the fantom hand.

His past, personal and family histories were irrelevant. Inquiry by systems did not elicit significant data.

Physical examination revealed a well developed man with an amputation stump of the right arm. A large, red, indurated area was present on the superior surface of the right shoulder caused by the excessive use of an ultraviolet light lamp. There was a posterior midline scar from the second cervical to the first thoracic vertebral spine. Palpation of the amputation stump caused a painful feeling, but neuromas were not present. Neurologic examination likewise showed few abnormalities. A small area over the tip of the right shoulder was anesthetic, and a larger area, extending from the third cervical to the third thoracic dermatome, was hypesthetic. Stimulation of this area, however, gave rise to a diffuse, disagreeable sensation, causing quick retraction of the shoulder.

On Feb. 19, 1942, 50 cc. of 1 per cent procaine hydrochloride was injected into the right brachial plexus, with temporary relief of pain, lasting less than two hours. Procaine block of the cervical portion of the right sympathetic chain, carried out on Feb. 20, 1942, aggravated the pain in the fantom hand.

On February 28 the patient was anesthetized with avertin (120 mg. per kilogram of body weight) with amylene hydrate. Along the line of the proposed horseshoe incision in the left occipital region 1 per cent procaine hydrochloride was injected. A small bone flap was turned down, being hinged by the occipital muscles. The dura was incised over the occipital lobe and a flap turned down along the lateral sinus. Several large veins passed into the sinus laterally, but so far from the field that it was possible to elevate the occipital lobe without cutting them. The tentorium was incised to the incisura. The arachnoid was then teased from the mesencephalon to expose the superior cerebellar artery, the trochlear nerve and the lateral surface of the mesencephalon. The inferior colliculus and its brachium were readily recognized, but the lateral sulcus was covered by several veins. An incision 5 mm. in depth was then made from the lateral sulcus across the brachium of the inferior colliculus. No bleeding occurred. The occipital lobe was allowed to fall back into place and the dura closed. The bone flap was replaced and the scalp closed with two layers of black silk.

The patient awoke two hours after the completion of the operation. The following day he stated that for a few hours his fantom limb had disappeared but that it was returning and becoming larger. It did not pain or burn. The entire right half of the body felt "dead" and was analgesic. Hearing was normal. The patient voided without difficulty. There was no motor weakness. Touch was well appreciated on the right side of the body. Incomplete right homonymous hemianopia could be demonstrated by gross tests.

On the second postoperative day he complained of a burning sensation in the right corner of the mouth, but this disappeared within twenty-four hours. His fantom arm was well formed but was not painful.

On the fourth postoperative day he felt fine. His visual acuity and fields were normal, but the patient stated that his vision was not quite "right." His right pupil was 4 mm. in diameter and the left 3 mm. Both reacted well to direct light. External ocular movements were full, and there was no nystagmus. Both corneal reflexes were active. There was no weakness of the masseter muscles. There were complete analgesia and thermanesthesia over the right side of the face. Occasionally pinprick on this side caused a peculiar sensation, which radiated into the right arm. Hearing was grossly normal. The motor power of the legs was equal and grossly normal. The tendon reflexes were active and equal on the two sides. The right abdominal reflexes were less active than the left. There were analgesia and thermanesthesia of the entire right half of the body, including the scrotum and penis. On

the tongue, however, pinprick appeared to be appreciated poorly but equally on the two sides.

On the sixth postoperative day the patient's condition was essentially unchanged. Cutaneous temperatures were taken after exposure in a room at a temperature of 21 C. (68.8 F.).

Site of Temperature Reading	Degrees (C.) Right	Left
Temple	33.5	34.5
Cheek	32.5	33.0
Shoulder	31.5	32.5
Chest	31.0	32.5
Flank	30.5	31.5
Thigh	29.5	29.5
Calf	29.5	29.5
Lateral malleolus	29.5	30.0
Great toe	28.5	29.5
Sole of foot	28.5	29.2

Von Frey hairs and pins were used to examine comparable areas on the face. A 6 Gm. pin was occasionally felt as sharp when applied to the right side of the face, but it did not "hurt." There was slight impairment of the appreciation of touch on the right side of the face. The significance of this observation is difficult to determine, since the preoperative testing gave a similar disparity (table 2).

TABLE 2.—*Number of Correct Responses to a Series of Forty-Nine Graded Tactile Stimuli Applied to a Square on the Cheeks*

Touch, van Frey Hair, Gm./Mm.	Before Operation		Six Days After Operation	
	Right	Left	Right	Left
0.5	3	1	14	37
1.0	18	28	35	34
2.0	19	40	42	46
3.0	35	46	47	48
5.0	47	..	..	..

On the seventh postoperative day audiometer readings showed a decrease in the perception of high tones (fig. 5). On the tenth postoperative day a cinema was taken to show the patient's neurologic status. Since the operation he had experienced occasional headaches, always on the left side. On the eleventh postoperative day he was given 0.1 mg. of histamine phosphate intravenously and experienced a severe, "bursting" headache on the left side of the head only. This lasted for eight minutes. Inhalation of amyl nitrite produced peripheral vasodilation but no headache. Prior to his operation both of these drugs had been ineffective in producing headache. On the sixteenth postoperative day examination of the peripheral visual fields and the blindspots revealed no abnormalities.

On the day of discharge, March 18, he was examined in detail by Dr. David Clark. The wound was well healed. The cranial nerves, with the exception of sensory fibers to the face, were normal. Gustatory stimuli were well appreciated. Cotton was accurately localized and equally appreciated on the two sides of the face. Pinprick was recognized only as a tactile impression on the right side of the face. Stimulation of the tongue with pinprick, however, was appreciated equally but poorly on the two sides. Pinprick was not appreciated on the right side of

the hard and the soft palate, although the palatal reflexes were brisk. The mouth being edentulous, sensation of the teeth could not be tested.

Although the right leg was said to feel weak, no impairment of strength could be detected clinically except that the patient hopped less agilely on the right foot than on the left.

Cotton wool was accurately localized and equally appreciated over the entire body. Position and vibratory sensibility and two point discrimination were normal. Tickle sense was normal on the two sides.

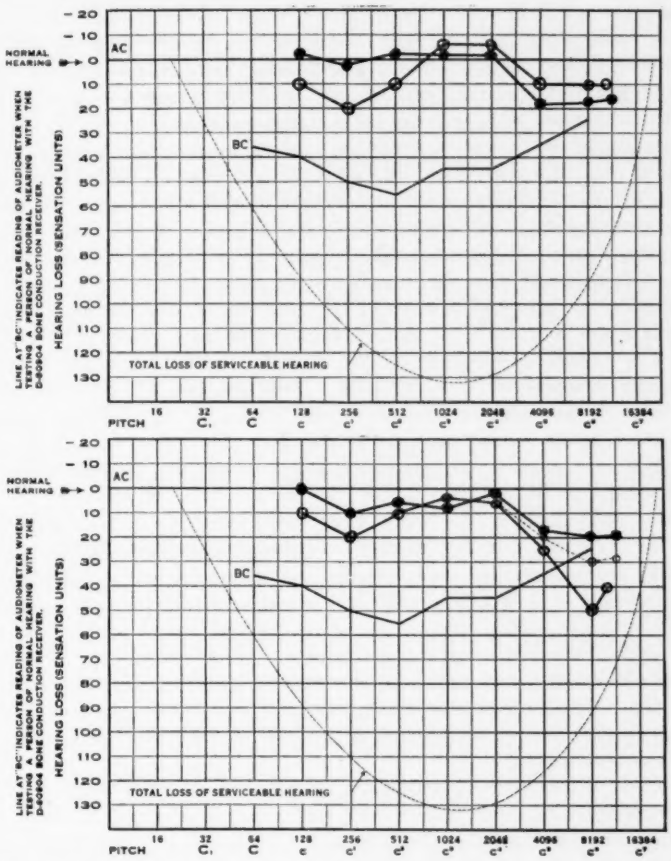

Fig. 5 (case 3).—Audiograms taken before (large dots) and two weeks after (heavy circles) mesencephalic tractotomy; those for the left ear are above and those for the right ear below. The light circles represent the observations three months after operation.

Both hot and cold stimuli were called warm, but could be distinguished with fair accuracy on the right side. Pinprick was felt as dull and was occasionally confused with cold stimuli. The head of the pin could usually be distinguished from the point, but the pain component of pinprick was absent. If, however, a skin clip was fastened in the skin of the right side, the patient experienced a diffuse, unpleasant sensation.

Compression and manipulation of the nerves of the right brachial plexus did not cause pain.

The patient returned June 1, 1942. For two weeks following his discharge he felt well. Then he began to experience a burning sensation on the right side of the face, the right flank and the right leg when he became tired or overexerted himself. At these times he had aching or cramping in the fantom arm. On awakening in the morning his arm and entire right side felt well, but after being up for a few hours, the burning sensation would appear. Noises were especially likely to bring on this paresthesia. If he lay down in a quiet room, the disagreeable sensation would pass away in a short time. The numbness in the right extremities disappeared five or six weeks after the operation. The right leg was not quite so strong as normal, and he limped slightly. Vision and hearing had been restored to normal shortly after his discharge. Libido, however, had not returned. In his opinion his condition was much improved over his preoperative state.

Examination showed that the patient's physical and mental states were unchanged from his first visit. He appreciated odors well in both nostrils. His visual acuity, visual fields and ocular fundi were normal. External ocular movements were full, and there was no nystagmus. The pupils were equal and regular and reacted well to direct and consensual light and in accommodation. The corneal reflexes were both active, the left being perhaps more so than the right. There was pronounced hypalgesia over the entire right side of the face, but a few patches existed in which pinprick was appreciated as such. Heat and cold were rarely felt other than as touch. The tongue and the gums did not share in the hypalgesia, and the palate seemed equally sensitive on the two sides. Deep pressure was less painful on the right side. When pinprick was appreciated it was felt as a diffuse, radiating sensation, which might extend over the entire right side. The remainder of the cranial nerves were normal. In particular, the cochlear and vestibular functions were unimpaired (fig. 5).

Over the right half of the body were pronounced hypalgesia and hypothermesthesia, so severe that only rarely was the stimulus appreciated for what it was. Rapidly repeated stimulation frequently produced a diffuse, unpleasant sensation, which was the same whether invoked by pinprick or the cutaneous application of a tube of ice water. Firm compression of the brachial plexus gave rise to pain, but compression of the bones was not distressing.

The appreciation of cotton wool was only slightly disturbed over the face, arm, trunk and leg. The localization of tactile stimuli was reasonably accurate, but slightly less so than on the corresponding parts of the left side. Vibratory and position senses were intact.

The strength of the right leg was slightly less than that of the left. The right abdominal reflexes were decreased, and the tendon reflexes of the right leg were slightly hyperactive as compared with those of the left leg. The right plantar response was equivocal and the left flexor. Rapidly alternating movements were well performed with both legs. No ataxia was apparent in the heel to knee test.

The patient's gait was steady, but he favored the right leg. He walked tandem unsteadily but could stand on either leg alone.

SEQUELAE OF MESENCEPHALIC TRACTOTOMY

Relief of Pain.—Immediately after the section, superficial or deep pain in the contralateral half of the body is relieved. Even if complete analgesia to pinprick is not present, the pain may be relieved, as in case 2. Abdominal pain on the involved side, such as might be produced by deep

palpation (case 1), is absent. Headaches, when they occur, are confined to the side of the head ipsilateral to the lesion. Even the headache produced by intravenous injection of histamine is mainly confined to one side.

Parasthesias.—The side of the body contralateral to the lesion feels "numb," "dead" or "funny" after the operation. After a time this sensation becomes less pronounced but does not disappear entirely. Although when questioned the patient speaks of this paresthesia, it is rarely complained of spontaneously. The third patient in this series stated that the numbness disappeared about a month after the operation, but he complained of a burning sensation, resembling causalgia in many respects, in the face, arm and leg on the hypalgesic side.

Analgesia and Thermanesthesia.—Immediately after the section, painful stimuli on the side of the body contralateral to the lesion are not appreciated. Pinprick is felt as touch and hot and cold objects as slightly warm. The sensory disturbance extends to the anatomic midline of the body or in a few areas—commonly about the mouth—reaches across the midsagittal plane. This sensory defect is so profound that towel clips may be clamped in the skin or hemostats hung on the webs of the fingers. Compression of the peripheral nerves and osseous structures is not painful.

After approximately two weeks pinprick gives rise to a peculiar, disagreeable feeling in the part stimulated. This same sensation may be elicited by cold, extreme heat or pinprick, particularly by repetitive stimuli, but the initiating stimulus cannot be identified. The sensation is not painful, but annoying—in fact, it is more unpleasant than pinprick on the normal side.

Mild Hypesthesia.—Touch does not seem to be impaired when tested with cotton wool, but when von Frey hairs are used a definite increase in the tactile threshold is demonstrated. Localization of touch, two point discrimination, vibratory sensibility, position sense and joint sense all appear practically normal.

Visual Disturbances.—For one or two days after operation hemianopsia contralateral to the lesion usually can be demonstrated grossly. Within a week, however, the visual fields are full. The visual acuity remains normal, but one patient stated, when questioned, that he did not see quite normally. Diplopia or nystagmus has not been seen.

Auditory Disturbances.—Although subjectively no auditory abnormalities were noted (except in case 3), in audiometer tests appreciation of high tones by the ear contralateral to the lesion is impaired. One patient (case 3) stated that his hearing was temporarily impaired in the involved ear.

Other Manifestations.—For a few weeks after operation the leg contralateral to the lesion is not so strong or agile as the ipsilateral leg. This becomes evident when the patient attempts to hop or stand on one leg. It usually passes away in about a month. The strength of the other extremities is normal. Even dynamometer readings fail to show any weakness. No ataxia can be demonstrated, even immediately after operation.

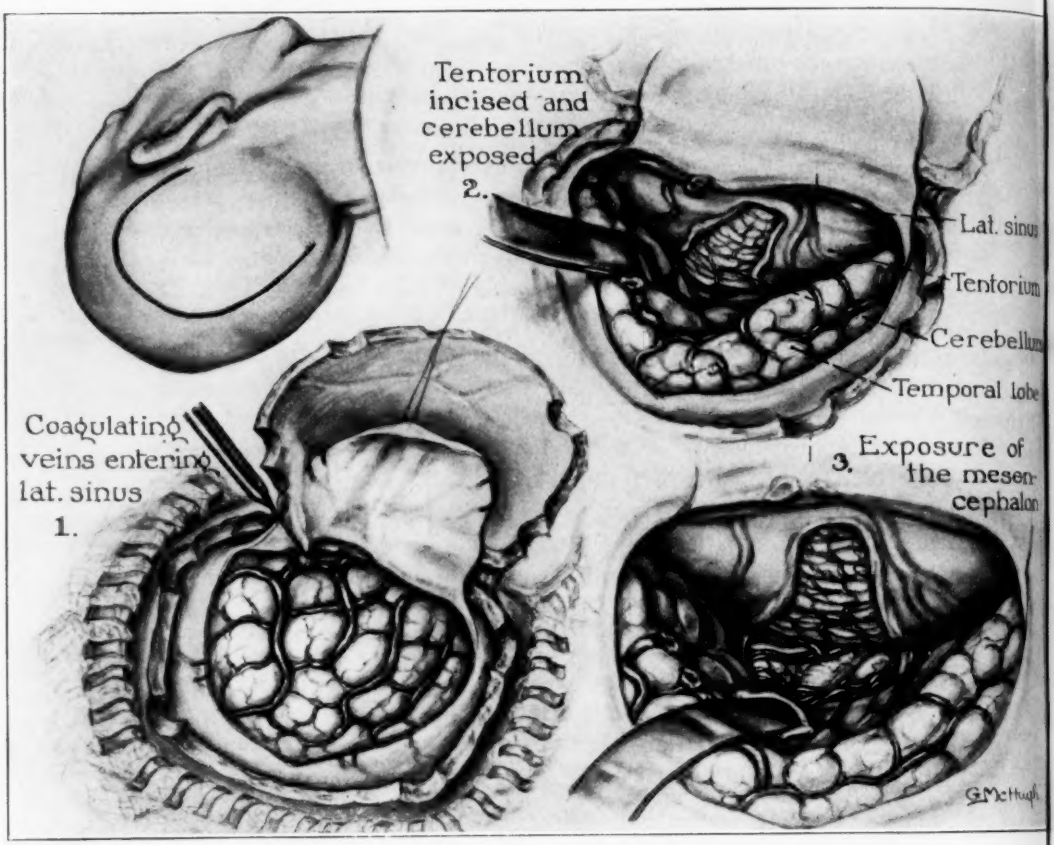

Fig. 6.—Sketches showing the operative approach for mesencephalic tractotomy.

No bladder disturbances are present unless the patient is confused or stuporous from some complicating factor, as in case 2. No statement regarding libido can be made at this time.

TECHNIC OF MESENCEPHALIC TRACTOTOMY

The operative field in which the section is made being limited at best, it is essential to use an anesthetic which does not produce intracranial

hypertension. Avertin with amylene hydrate and local infiltration of the skin along the line of the incision have been satisfactory. If this is supplemented by morphine sulfate, ⅙ grain (0.010 Gm.), an excellent basal anesthesia is insured without a rise in blood pressure or intracranial hypertension. A horseshoe-shaped incision is made in the occipital region opposite the painful lesion. The medial limb of the incision should begin 3 cm. below and 1 cm. medial to the external occipital protuberance, pass vertically upward for 6 cm. and curve laterally and then downward to end just below and medial to the mastoid

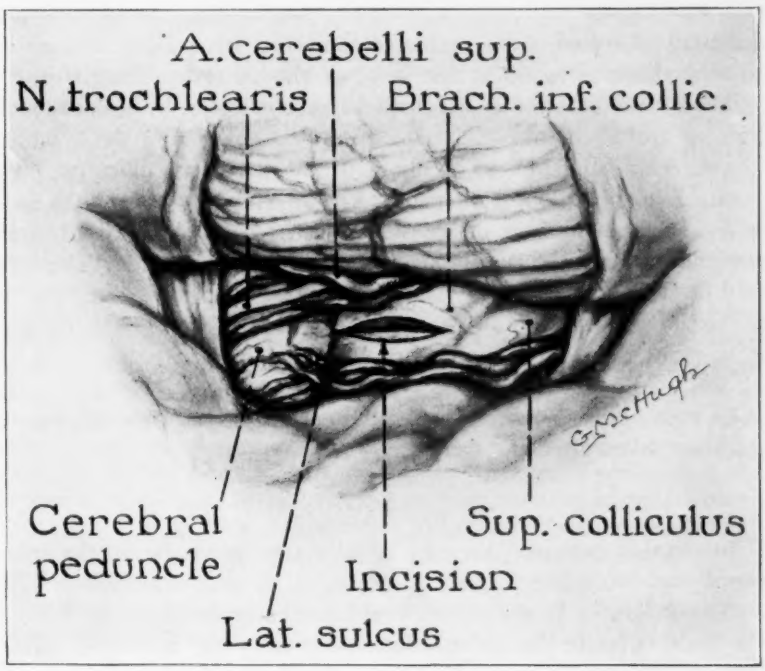

Fig. 7.—Sketch showing the landmarks for the incision.

process. Four perforations are then made for the bone flap, the two inferior being in the occipital bone just below the lateral sinus and the two superior 4 to 5 cm. above the lateral sinus. The bone between the perforations is cut with the Gigli saw, except the base, which is fractured. The line of fracture should be just below the lateral sinus. If it is not, the bone should be rongeured away to expose the sinus. The dura is then incised and a flap turned down with the base at the lateral sinus. Usually one or two large veins will be seen passing into the sinus in the middle of the field and will have to be coagulated and cut. However, on two occasions I have been able to expose the mesencephalon

without cutting any vessels passing into the lateral sinus. The occipital lobe, protected by cottonoid strips, is then elevated to expose the tentorium. The latter is incised to the incisura. If the cisterna ambiens, which is exposed by this maneuver, is punctured and a cottonoid pad left in the angle between the occipital lobe, the mesencephalon and the cerebellum for a few minutes, adequate space for exposure of the mesencephalon will be gained. The arachnoid is then teased from the anterior margin of the cerebellum, exposing the trochlear nerve and the superior cerebellar artery. Usually a fine venous plexus lies over the lateral surface of the mesencephalon, but these vessels can be gently pushed to one side to expose the colliculi, the brachium of the inferior colliculus and the lateral sulcus of the mesencephalon (fig. 6).

The incision is made at the level of the posterior margin of the superior colliculus from the lateral sulcus (about 5 mm. from the anterior margin of the brachium pontis, which is not seen) across the brachium of the inferior colliculus to the base of the superior colliculus. The incision, 5 mm. in depth, is made by a sharp-pointed, straight knife (fig. 7). Such a knife is necessary, since the operator's line of vision is at right angles to the lateral surface of the mesencephalon. The knife should be passed through the incision a second time to be sure that all fibers have been cut. No bleeding is usually encountered. The occipital lobe is replaced and the skin margins closed with two layers of the black silk.

The postoperative course is usually uneventful, and only the routine precautions taken after any craniotomy are necessary.

SUMMARY

Unilateral intractable pain may be alleviated by section of the spinothalamic and secondary trigeminal tracts at the mesencephalon. This procedure produces hemianalgesia and hemithermanesthesia on the side of the body opposite the lesion immediately after the operation, with a peculiar feeling of "numbness" or "deadness." There is slight weakness of the contralateral leg, demonstrable only by having the patient hop or stand on that leg alone. Coordination is normal. Proprioceptive sensibilities are not impaired.

University of Chicago Clinics.

ABSTRACT OF DISCUSSION

DR. FRANCIS C. GRANT, Philadelphia: Pain and its relief is an important problem. Chordotomy at the level of the first thoracic segment will relieve any variety of pain below the ensiform cartilage. Section of the posterior roots of the fifth and ninth cranial and upper four cervical nerves will check pain referred to any point between the vertex and the level of the clavicle. But pain in the shoulder, axilla, arm or hand due to infiltration or irritation of the lower cervical

roots or the brachial plexus presents a more complicated problem. Section of posterior roots from the fourth cervical to the second thoracic segment will produce complete anesthesia to all forms of sensation from the shoulder and axilla to the finger tips, but, curiously, is amazingly ineffective in relieving the distress. The original pain may be much reduced, but the patient has a numb, heavy, entirely useless and eventually partially spastic limb. In my experience the presence of the useless limb, with its consequent weight and drag on the shoulder, has set up a train of complaints—burning and paresthesias in the hand, arm and neck—which have been essentially as annoying to the patient as the original pain.

High cervical chordotomy at the level of the second cervical segment affords a second solution to relief of pain in the upper extremity. My associates and I have used this procedure in 7 cases, with really satisfactory results in 3, fair results in 2 and unsatisfactory results in 2. In both the cases in which the results were unsatisfactory and in 1 of those in which the outcome was fairly satisfactory posterior root section was added to the chordotomy to be sure that the anesthesia was brought up to a sufficiently high level. I feel that this combination accounts for the unsatisfactory results, for the complete loss of sensation in part of the arm and hand consequent on posterior root section carried with it the paresthesias which seem to accompany root section and impaired the result. If high cervical chordotomy is done without root section, the relief of pain is satisfactory. There is no interference with touch or muscle sense; the function of the arm is not impaired; subjectively sensation is not changed, and the patient is not conscious of any difference in the feeling of his arm except for relief of pain. But section of the cord at the second cervical segment does not seem so simple as section at a thoracic level; the cord looks thick and formidable; the nerve roots lie close together, with many vessels on the surface of the cord. A much deeper section is required, and the thought of phrenic and intercostal paralysis is always present in the mind of the conscientious operator.

I have never carried out section of the sensory tracts in the medulla, as suggested by Schwartz and White. From a small experience with section of the descending root of the trigeminal nerve, I know the hazards inherent in surgery in that area. I much prefer high cervical chordotomy to section of the tract in the medulla. We have had occasion fairly frequently to section the tentorium up to the incisura. This region is well known to the neurosurgeon in cases in which amputation of the occipital lobe is indicated in removal of a tumor in this area or in approach to a tumor of the pineal body.

In the case of a pulmonary cancer with supraclavicular metastasis I carried through Dr. Walker's procedure to the best of my ability. The approach to the peduncle is easy, the only difficulty consisting in freeing the overlying subarachnoid veins and ascertaining with confidence just where, at what angle and to what depth the section should be made. I found it difficult to discover an avascular area on the surface of the peduncle through which a bloodless section could be performed. Further experience will clear up these points. I feel that Dr. Walker has presented a practical method for relief of pain in the upper extremity. I do not believe, nor do I suspect that he feels that his operation is to be preferred to high thoracic chordotomy for, say, pain in the leg due to pelvic cancer.

The results in my case were interesting. Objectively, there could be demonstrated only mild hypalgesia down to the level of the sixth thoracic segment, including the whole right upper extremity, but not the face. Ordinary touch, position and vibratory sensations seemed unimpaired. Thermalgesia was present to the same slight degree as loss of pain. I had put the result down as a failure

due to my inexperience with the procedure. But although the patient had required 1½ grains (0.097 Gm.) of morphine sulfate every four hours to obtain any reasonable comfort, ten days after operation he needed but ½ grain (0.032 Gm. of codeine and 10 grains (0.65 Gm.) of acetylsalicylic acid every six hours for complete comfort and was extremely satisfied with the result. Other than to state that I know pain when I see it (the supraclavicular region was hardened with cancer and tissue formed in reaction to roentgen rays, and his arm was badly swollen, so that he had every reason to have the suffering of which he complained) and that I am sure his distress was not functional, I have no explanation for his great relief with so little sensory loss.

I congratulate Dr. Walker on his courageous persistence in pushing through a difficult clinical investigation to such a successful conclusion.

Dr. Max M. Peet, Ann Arbor, Mich.: I have been interested for many years in the relief of pain and have been gratified by the results which are obtained in the lower extremity with chordotomy. But the relief of pain in the upper extremity, in the cervical region and even in the upper part of the chest has been a discouraging problem. My colleagues and I have done chordotomies at the second cervical level, with entirely satisfactory results in some cases and with complete failure to relieve the pain in the arm in others, or the level perhaps would be up to, or even overlapping, the area where the patient complained of pain. I was happy when Schwartz and White first presented a method for tractotomy in the medulla, and Dr. Walker has described a still higher chordotomy. To get relief in many cases of high thoracic or low cervical pain we have almost universally been combining rhizotomy with chordotomy, that is, cutting the second, third and fourth posterior roots, which gives anesthesia, of course, of the upper portion of the arm and shoulder. That worked well in some cases; it had no effect, apparently, in cases of fantom arm. I therefore tried Schwartz's operation, medullary tractotomy, in 3 cases. One was a case of very severe pain, of unknown origin, in the arm or shoulder, extending into the hand, in treatment of which I had satisfactory results. The second was a case of fantom arm, and although at the time I obtained satisfactory relief of pain, just before I left to come to this meeting, I had word from the attending physician that he was sending the patient back with her original complaint. The third was a case of excruciating, continuous pain in the arm and hand of known central type. I should like to ask Dr. Walker whether he thinks that his high chordotomy would give relief from pain of this type. All see cases of this kind. In some the pain is due to cerebral softening; in some, to thrombosis, and in some the cause is unknown. If this operation, which is apparently reasonably safe, can offer anything in relief from such pain, it is worth trying. I wonder how much complaint patients with pain only, say in the shoulder and arm, may have if they also lose sensation of pain in the face. Ordinarily, loss of pain sensation does not mean much, but some of the patients apparently have paresthesia; that is, they complain that a painful stimulus produces a more unpleasant sensation than the pain itself, or than the pain created on the opposite side by pinprick. So I wonder whether some of the complications which occurred after most procedures for postinsula control or for relief of trigeminal neuralgia may not appear after this operation. This work of Dr. Walker deserves commendation. His is the first case to be reported of high cervical chordotomy, rather than of high cervical chordotomy plus rhizotomy, for relief of upper thoracic pain.

Dr. Paul C. Bucy, Chicago: I should like to mention two points in connection with Dr. Walker's excellent presentation. It has been common experience—

not mine, for I have not had any—that with Dr. Schwartz' operation of sectioning the spinothalamic tract in the medulla oblongata the level of analgesia has not extended above the clavicle. Both Dr. Schwartz and Dr. White reported having had that experience, whereas with Dr. Walker's method the level is much higher and therefore the results are much better in patients suffering from pain in the upper extremity, neck and face.

The other point is of a different nature. One has been taught and still frequently finds in the literature the statement that sensory loss from real organic lesions is not strictly in the midline of the body and that such loss is indicative of hysteria. I think that for once and all Dr. Walker has laid that ghost and demonstrated that loss of sensation of organic origin may be strictly in the midline.

Dr. A. Earl Walker, Chicago: I am grateful to the discussants for raising a number of interesting points. I agree with Dr. Peet that if paresthesias are the result of this procedure, they will negate the value of the operation. That is one reason that I do not as yet know the indications for the procedure, and it will probably be several years before one can determine the type of case in which this operation will be most valuable. Perhaps a differential section of the pain fibers, care being taken to leave intact those, shall I say, of the lower extremity or of the face, or perhaps even of the arm, if one wishes merely to section the fibers from the neck and face, might minimize the possibility of distressing paresthesias.

Dr. Peet asks whether such a procedure, interruption of the secondary pain fibers at the level either of the medulla or of the mesencephalon, might relieve central pain. I think it is possible, but I should not be at all surprised if a certain amount of pain persisted. In my opinion, the relief would occur because fewer peripheral impulses were coming through. It is common experience that patients suffering from central pain experience more distress when they are receiving impulses from the peripheral portions of the body, although they may have pain at other times as well. It is possible that relief from this central pain may be obtained by excision of a portion of the postcentral region of the cerebral cortex.

Dr. Grant referred to the difficulty in separating the vessels on the surface of the mesencephalon. However, with care and gentleness one can usually, by means of cottonoid patties, push the vessels to one side so as to uncover a relatively avascular area on the brachium of the inferior colliculus.

It must be emphasized that this procedure is still in the experimental stage. The indications for it and the sequelae can be determined only after operation in a relatively large number of cases. It merits such trial since it offers a method for the relief of pain which previously could not be satisfactorily treated.

SOMATOTOPIC LOCALIZATION OF SPINOTHALAMIC AND SECONDARY TRIGEMINAL TRACTS IN MESENCEPHALON

A. EARL WALKER, M.D.
CHICAGO

Surgical interruption of the pain pathways in the mesencephalon demands an accurate knowledge of the position of the spinothalamic and secondary trigeminal tracts. While considerable data have been accumulated on this point, there is practically no information on the topical localization of the spinothalamic tracts in the mesencephalon.

PRESENT INVESTIGATION

In an attempt to determine the arrangement of the spinothalamic and secondary trigeminal tracts in the mesencephalon the following operations were performed on 4 monkeys (Macaca mulatta).

Experiment 1: A lesion of the spinal nucleus of the trigeminal nerve.

Experiment 2: A midline myelotomy from the twelfth thoracic to the first lumbar segment.

Experiment 3: A midline myelotomy from the fourth cervical to the sixth cervical spinal segment.

Experiment 4: A midline myelotomy from the fifth lumbar to the seventh lumbar segment.

The animals were killed two to three weeks after operation and the brains placed in Müller's fluid.

The extent of the lesion was confirmed by examining Marchi preparations taken from one segment above the lesion. The upper part of the pons and entire mesencephalon were treated according to Marchi's technic and sectioned serially, every section being mounted.

Photomicrographs were made of the brain stem at three levels, the decussation of the fourth nerve, the inferior colliculus and the caudal part of the superior colliculus, and on these photomicrographs the degeneration was marked (figs 1, 2 and 3).

TOPICAL ARRANGEMENT OF THE PAIN PATHWAYS

At the rostral margin of the brachium pontis the fibers of the spinothalamic and secondary trigeminal tracts reach the periphery of the brain stem near the lateral sulcus. Textbook descriptions of these pathways

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in the mesencephalon are rather indefinite. It is frequently stated that these fibers run in the medial lemniscus. However, studies of Marchi degeneration in the monkey, chimpanzee and man (Walker [1]; Rasmussen [2]) have shown that these tracts lie among the fibers of the lateral lemniscus. At the point of their emergence from the tegmentum they turn dorsally to lie on the periphery of the brain stem. They pass through the base of the inferior colliculus, some of their fibers terminating in that nucleus and the remainder passing either external or internal to the nucleus of the inferior colliculus to lie closer to the surface of the mesencephalon, just beneath the brachium of the inferior colliculus. These fibers do not enter the brachium. They ascend in the brain stem, maintaining their position medial to the brachium of the inferior colliculus to the point at which the latter enters the medial geniculate body. The spinothalamic and quinto (trigemino) thalamic tracts pass rostrally on the medial surface of the corpus geniculatum mediale to reach its dorsal surface. At this point they turn laterally to enter the nucleus ventralis posterior of the thalamus.

In the mesencephalon there is a certain topical organization of these tracts. Although there is no absolute separation of the fibers from the different spinal segments, there are two general principles of topical localization. The first is a mediolateral lamination, in which the fibers from the more caudal segments of the body tend to lie peripherally and those from the rostral segments to lie medially in the mesencephalon. Thus, at the level of the inferior colliculus the fibers from the cervical segments assume a position along the medial aspect of the inferior colliculus, whereas the fibers from the lumbar region lie on the periphery (fig. 2). As mentioned previously, this is not an absolute relationship, for there does not appear to be an appreciable difference between the position of the fibers from the lower thoracic region and those from the lower lumbar levels.

The second mode of orientation is a dorsoventral arrangement, in which fibers from caudal segments lie dorsal in the lateral lemniscus to those from rostral segments. Thus, at the level of the emergence of the trochlear nerve the fibers from the lumbar segments lie just ventral to the trochlear nerve and dorsal to the nucleus of the lateral lemniscus, whereas the fibers from the spinal nucleus of the fifth nerve lie at the

1. Walker, A. E.: The Spinothalamic Tract in Man, Arch. Neurol. & Psychiat. **43**:284-298 (Feb.) 1940.

2. Rasmussen, A. T.: The Lateral Spinothalamic Tract and Associated Fibers of Man, Anat. Rec. **79** (supp. 2):51, 1941.

level of the lateral sulcus of the mesencephalon (fig. 1). Further rostrad the lumbar fibers are covered by the brachium of the inferior colliculus, but remain superficial and dorsal to the fibers from the spinal trigeminal nucleus (fig. 3).

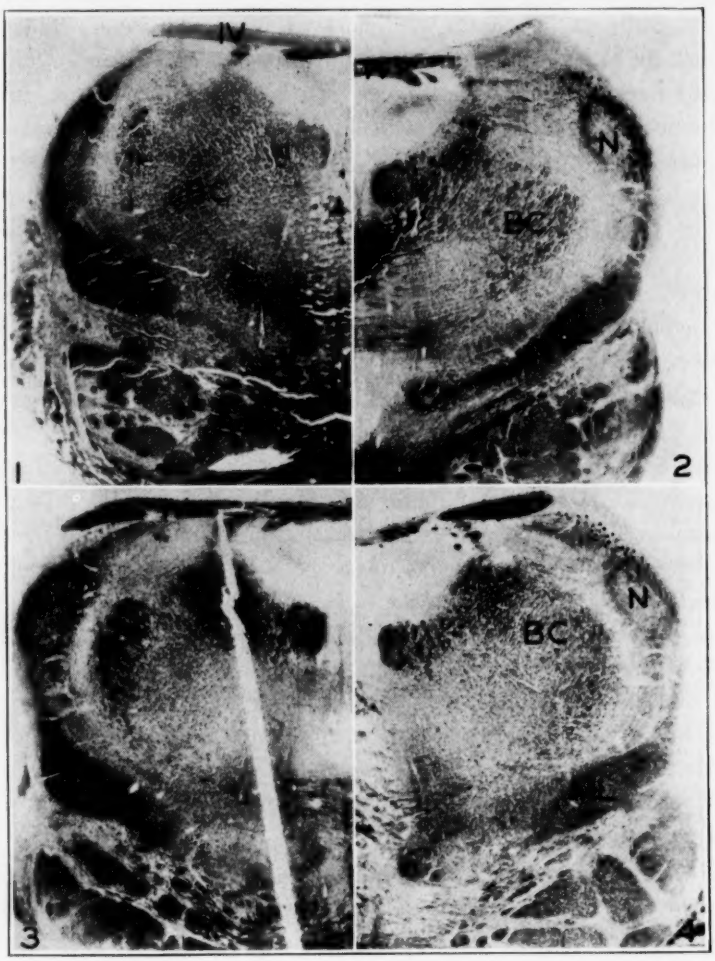

Fig. 1.—Sections from the level of emergence of the trochlear nerve, showing the position of Marchi degeneration after the following experimental procedures: (*1*) a lesion of the spinal trigeminal nucleus; (*2*) a midline myelotomy between the twelfth thoracic and the first lumbar segment; (*3*) a midline myelotomy between the fourth and the sixth cervical segment, and (*4*) a midline myelotomy between the fifth and the seventh lumbar segment.

The somatotopic arrangement of the pain pathways at this level is apparent.

In this figure, and in the accompanying figures, *B C* is the brachium conjunctivum; *M L*, the lemniscus medialis; *N*, the nucleus lemnisci lateralis, and *I V*, the nervus trochlearis.

It will be noted that at the level of the inferior colliculus the fibers from the lowest segments lie on the lateral and inferior surfaces of the colliculus, whereas those from the cervical segments and the spinal

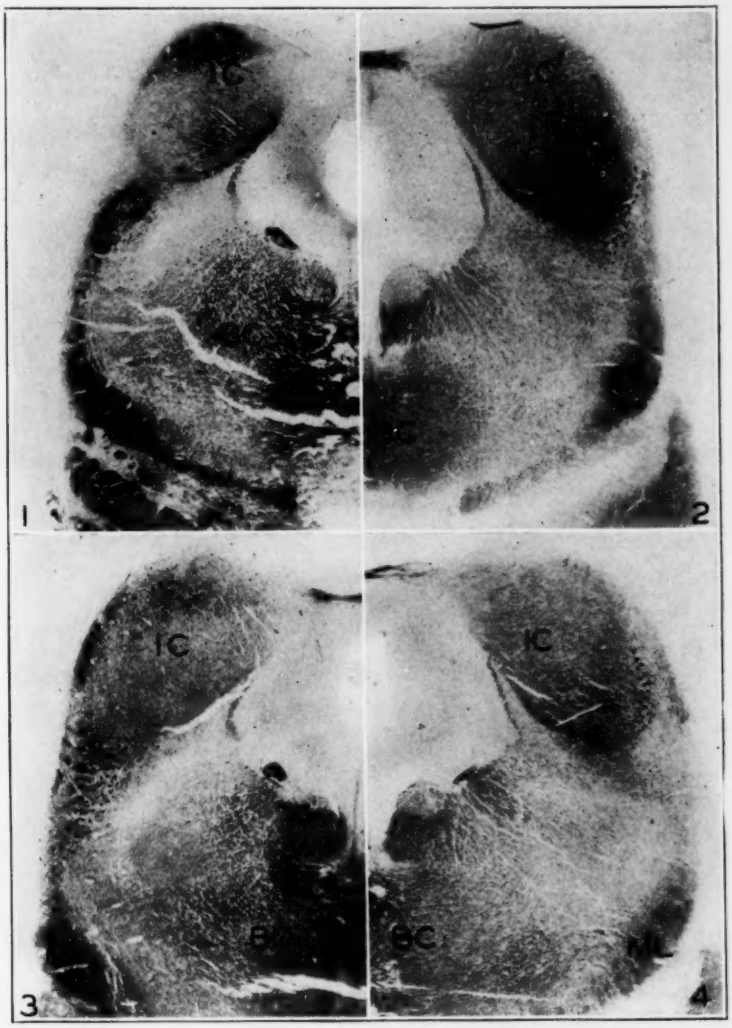

Fig. 2.—Sections from the level of the inferior colliculus and nucleus of the fourth nerve, showing the somatotopic orientation of the pain pathways. The numbers indicating the lesions are the same as those in figure 1. *I C* indicates the colliculus inferior.

trigeminal nucleus are on the inferior and medial aspects of the colliculus (fig. 2).

COMMENT

The topical localization of the secondary pain pathways within the mesencephalon has received little clinical attention. In the recent surgical sections [3] of these tracts at this level, it has been found that planned,

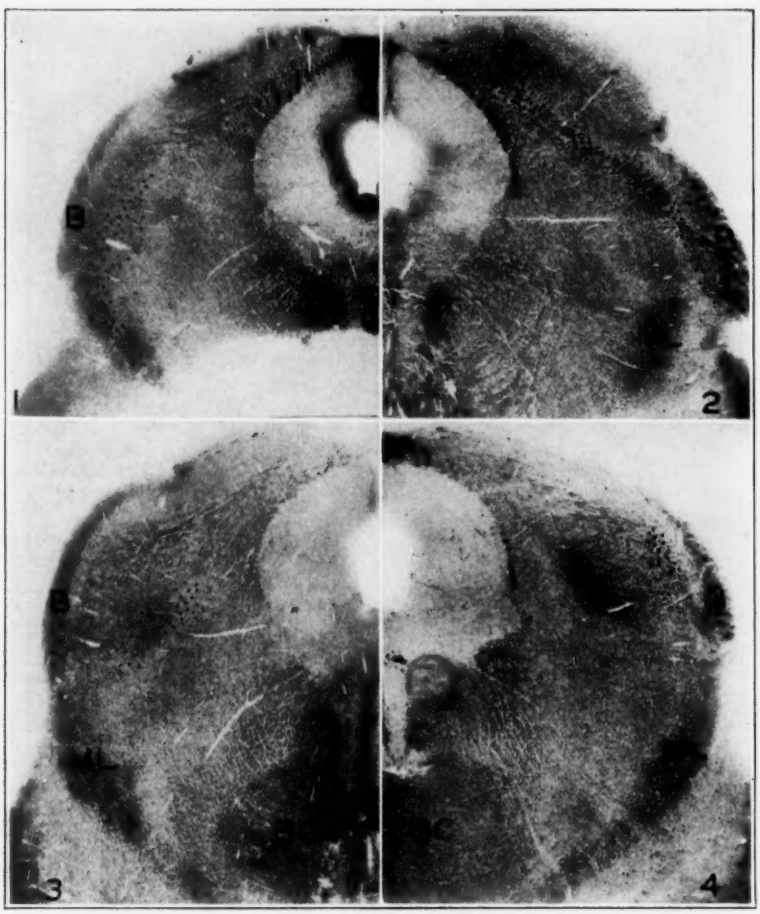

Fig. 3.—Sections through the superior colliculus, showing the somatotopic orientation of the pain pathways. The numbers indicating the experimental lesions are the same as in figure 1. *B* indicates brachium quadrigeminum inferius.

incomplete sections will give rise to monoanalgesia. Thus, an incision from the lateral sulcus to a point halfway through the brachium of the inferior colliculus gave rise to pain and thermal disturbances only over

3. Walker, A. E.: Relief of Pain by Mesencephalic Tractotomy, Arch. Neurol. & Psychiat., this issue, p. 865.

the face, arm and upper part of the thorax.[3] It is probable that this represents a differential section of the pain pathway, although conceivably bilateral representation in the thalamus could account for the sensory disturbances. It is interesting to note that in these cases the sensory impairment was not absolute or permanent, a fact which is in line with the intermingling of fibers from different segments of the spinal cord.

The orientation of the pain fibers in the mesencephalon is perhaps an expression of their final disposition in the thalamus and an example of neurobiotaxis. It has been shown that the fibers from the lumbar segments of the spinal cord tend to end in the lateral parts of the nucleus ventralis posterior of the thalamus, while those from the spinal trigeminal root terminate medially. This arrangement, like the other topical organizations, is not an absolute one, and there is much apparent, if not real, overlap of adjacent segments. A similar somatotopic orientation in the mesencephalon might well illustrate the principle of neurobiotaxis.

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PROBLEM OF IMPERCEPTION OF DISEASE AND OF IMPAIRED BODY TERRITORIES WITH ORGANIC LESIONS

RELATION TO BODY SCHEME AND ITS DISORDERS

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UNAWARENESS OF DISEASE

There is a group of patients affected with cerebral hemiplegia, usually of the left side, who show the strange feature of lack of awareness of their own defect. Not only do such patients tend to behave as though they could move their disabled limbs perfectly, but they deny their paralysis altogether. The phenomenon is observed not rarely if looked for. Its occurrence seems to depend on the mode and rapidity of onset of the defect rather than on its extent and severity. The more sudden the onset, the more likely is the symptom to occur. The condition is usually transient, but may sometimes persist for a longer or shorter period, even until death. The phenomenon of nonperception of disease has also been observed in patients with cortical blindness from bilateral lesion of the occipital lobe. Besides, it has been noted in persons with visual field defects from tumors in the sella region and in patients with left-sided cerebral hemianopia. Occasionally it has been seen in cases of peripheral blindness following primary optic nerve atrophy. The phenomenon has, furthermore, been observed in cases of cortical deafness resulting from bilateral lesion of the temporal lobe. Another—rather common but not generally appreciated—instance of unawareness of one's own defect is demonstrated by certain forms of aphasic disorder, especially of the receptive, paraphasic and syntactic types. The best known example, however, of nonrealization of one's own defect is represented by the so-called fantom limb, consisting in the experience of possession of a lost member of the body.

Already in 1885 von Monakow [1] had described the phenomenon of nonrealization of disease in a case of cortical blindness. This observation

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This paper was read in abstract at the Ninety-Eighth Annual Meeting of the American Psychiatric Association, Boston, May 19, 1942.

From the Department of Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Service of the First Division, Welfare Hospital.

1. von Monakow, C.: Experimentelle und pathologisch-anatomische Untersuchungen über die Beziehungen der sogenannten Sehsphäre zu den infrakortikalen Opticuscentren und zum N. opticus, Arch. f. Psychiat. **16**:151 and 317, 1885.

was confirmed by Rieger and Wolff (1892) and by Dejerine and Vialet [2] (1893). In 1898 Pick [3] reported the case of a patient having left cerebral hemiplegia of the existence of which he was unaware. But Anton [4] (1899) was the first to emphasize the problem of nonperception of disease with certain organic defects and to show its connection with localized cerebral lesions, describing the condition in cases of left hemiplegia, as well as in those of cortical blindness or deafness. Yet it was not until 1914 that the phenomenon of unawareness of disease aroused wide interest, when Babinski [5] reported the cases of 2 patients suffering from left cerebral hemiplegia of which they were not conscious. Babinski called the phenomenon anosognosia, that is, lack of knowledge or recognition of disease. This is rather a general term applied to a specific type of agnosia. Nonperception of hemiplegia may, however, be regarded as one aspect of unawareness of disease, since the phenomenon, as already mentioned, is known to occur in cases with certain other forms of somatic defect and, moreover, in those not only of central but of peripheral origin. It is in this sense that the use of the term anosognosia appears accurate. Unfortunately, the term has become already established in the literature for nonrealization of hemiplegia. Cases were even categorized under that term which differed from those of Babinski in that not only the paralysis but the affected limbs or side of the body had been unrecognized or had disappeared out of the patient's awareness.

SYMPTOMATOLOGY OF IMPERCEPTION OF HEMIPLEGIA AND CLASSIFICATION OF THE VARIETIES OF THE CONDITION

In this paper I am mainly concerned with the hemiplegic patient who shows unawareness of his paralysis. The hemiplegia is usually of the left side of the body. The patient behaves as though he knew nothing about his hemiplegia, as though it had not existed, as though his paralyzed limbs were normal, and he insists that he can move them and can walk as well as he did before. Asked to lift up both arms, he naturally moves the healthy one only, but maintains that he has raised the disabled one also. Requests for movements with the paralyzed left arm or leg are performed by him merely with the healthy one, or not at

2. Dejerine and Vialet: Contribution à l'étude anatomo-pathologique des différents variétés de cécité verbale, Compt. rend. Soc. de biol., 1893.

3. Pick, A.: Beiträge zur Pathologie und pathologischen Anatomie des Centralnervensystems mit Bemerkungen zur normalen Anatomie desselben, Berlin, S. Karger, 1898.

4. Anton, G.: Ueber Herderkrankungen des Gehirns die vom Patienten selbst nicht wahrgenommen werden, Wien. klin. Wchnschr. **11**:227, 1898; Ueber Selbstwahrnehmungen der Herderkrankungen des Gehirns durch den Kranken bei Rindenblindheit und Rindentaubheit, Arch. f. Psychiat. **32**:1, 1899.

5. Babinski, J.: Contribution à l'etude des troubles mentaux dans l'hemiplégie organique cérébrale (anosognosie), Rev. neurol. **22**:845-848, 1914.

all, but at the same time he is convinced that he has carried out the task. The patient may pay no attention to the paralyzed side, as though he had forgotten it; some not only neglect the defective side, but even refuse to look at it or turn away to the right. If such a patient is shown the affected arm or leg as being attached to his body, he will often remain indifferent or will declare that it is not his or that some one else's is in his bed, and the like. It is as though the patient experienced the paralyzed limbs as absent. Various illusions, distortions, confabulations and hallucinatory or delusional ideas may be produced in this connection.

A hemiplegic patient of Zingerle's [6] had peculiar erotic experiences through contact with the "absent" left limbs, which he believed were those of a woman. A patient of Pötzl's [7] with left hemiplegia said of his paralyzed arm: "I don't know where it comes from; it is so long and lifeless and as dead as a snake." He would often complain that a strange person was on his left side in the bed and was trying to push him away. Another hemiplegic patient of Pötzl's felt that his left arm was estranged and separated from his body. A patient of Nielsen's [8] (speaking of her left hemiplegic extremities) declared: "That's an old man. He stays in bed all the time." On being questioned whether she did not mind, she replied: "Yes, I don't want spirits in bed with me. That's my brother-in-law's hand." A patient observed by Ives and Nielsen [9] said: "Some one is substituting this arm [pointing to the left, or paralyzed, one] for my left arm," and "My wife rubbed this arm, but it wasn't my arm." Of particular interest is a case of left hemiplegia described by Olsen.[10] His patient denied that the affected limbs were hers and said that "yours" or another's were in bed with her. When they were shown to her as being connected with her own body, she stated: "But my eyes and my feelings don't agree, and I must believe my feelings. I know they look like mine, but I can feel they are not, and I can't believe my eyes." This observation seems to me significant, especially for its suitability to indicate a certain dissociation by disease of the body scheme into its tactile-kinesthetic and its optic constituents.[11]

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6. Zingerle, H.: Ueber Störungen der Wahrnehmung des eigenen Körpers bei organischen Gehirnerkrankungen, Monatschr. f. Psychiat. u. Neurol. **34**:13-36, 1913.

7. Pötzl, O.: Ueber Störungen der Selbstwahrnehmung bei linksseitiger Hemiplegie, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:117-168, 1925.

8. Nielsen, J. M.: Gerstmann Syndrome: Finger Agnosia, Agraphia, Confusion of Right and Left and Acalculia; Comparison of This Syndrome with Disturbance of Body Scheme Resulting from Lesions of the Right Side of the Brain, Arch. Neurol. & Psychiat. **39**:536-559 (March) 1938.

9. Ives, E. R., and Nielsen, J. M.: Disturbance of Body Scheme: Delusion of the Absence of Part of Body in Two Cases with Autopsy Verification of Lesion, Bull. Los Angeles Neurol. Soc. **2**:120-125, 1937.

10. Olsen, C. W., cited by Nielsen.[8]

11. The concept of the body scheme will be dealt with in a subsequent paragraph.

As I have said before, the syndrome under discussion has proved not to be rare when searched for. A considerable number of competent observations have been reported in the literature. I myself have noticed its presence in a series of cases of cerebral lesion. Two cases presenting different types of the syndrome which I have recently observed [12] seem particularly worthy of report.

CASE 1.—*History of sudden development of left hemiplegia in April 1941. Spastic left hemiparesis with typical manifestations. Impaired sensory perception on the left side, affecting proprioceptive, epicritic and protopathic sensibility in various degrees. Thalamic type of sensory disorder. Hyperpathia, spontaneous pains, dysesthesias and paresthesias, irradiations, etc. Anosognosia for left hemiplegia, but no disturbance of awareness of the affected limbs as such. Since onset of the disease, episodes of a peculiar illusional experience, as though some one else's arm or hand, casually held in front of her, were the patient's own paralyzed one. No mental impairment. No other disorder.*

J. M., a single white woman aged 48, right handed, an artist, was admitted on July 24, 1941 with a history of having had a rather sudden onset of left hemiplegia in April 1941. Paralysis was preceded one week by a severe pain in the nasion, numbness on the left side of the head, flashes of light and blurring of vision.

On the day of onset the patient felt weak, ill and apprehensive. She lay down on a couch to rest and shortly thereafter suffered a severe spasm in both legs. She could not straighten them immediately; so she swung around to a sitting position and, in attempting to rise, fell to the floor on her left side. She realized that something had happened to her, but did not appreciate the change as paralysis of her left side [13] and continued in futile attempts to walk and use her left arm and hand. During a physician's examination that evening, and for the next two days in a hospital, she was unaware of the fact that her left arm and leg were paralyzed, although she knew by that time that their use was limited. She was somewhat chagrined but not particularly worried. The realization of the paralysis, as such, did not occur until the third day and was then received with quite a shock.

The following interesting observation deserves notice. At times since the onset of the paralysis, when the patient has seen other persons in front of her in the casual position of placing the arm or hand to the face or chest, but not in contact with her, she has experienced an obsessive feeling that the healthy extremity belonging to some one else was her own left, paralyzed one. The matter of distance enters into this illusional situation, for the person must be near enough to her to make the experience possible.

Neurologic examination revealed spastic left hemiplegia with involvement of the lower left part of the face and typical signs and symptoms. Sensory disturbances on the left side showed distinct thalamic characteristics of diffuseness, irradiation with a sense of vibration, reduced acuity of perception and excessive reaction to painful stimuli, with pronounced affective coloring in terms of hyperpathia, spontaneous pains and a sense of pulling and itching on the left side. The area of irradiation tended to assume the form of a circle and was felt as about the same in both the distal and the proximal parts of the affected extremities. Besides, there was a peculiar perversion of sensation, in which pain and coldness

12. These cases were studied in the neurologic service, First Division, Welfare Hospital.

13. The patient stated that she knew well what paralysis was, but she simply did not think of her difficulty in those terms.

were associated and were often interchanged or reversed. Warmth and touch showed a similar association. Examination of epicritic and deep sensibility revealed rather severe impairment of cutaneous localization, two point discrimination, position sense, perception of passive movements and vibratory sensation, more prominent distally and in the upper extremity. There was marked astereognosis.

The diagnostic impression was that of a thrombotic lesion affecting the right thalamus and its cortical radiation, especially the thalamoparietal peduncle.

CASE 2.—*History of heart disease, hypertension and a positive Wassermann reaction of the blood. Sudden onset of left hemiplegia in April 1941. Association of hemiplegia, with impairment of proprioceptive, epicritic and protopathic sensation on left side and with disturbance of perception in the left visual field. Thalamic-like features of sensory disorder. No clouding of consciousness. Tendency of head and body to deviate to the right, but no material weakness of conjugate movements of the eyes to the left. Complete anosognosia for left motor and sensory disturbances; amnesia and agnosia for and denial of possession of the left (affected) limbs; formation of illusional, confabulatory and delusional ideas concerning them. Gradual recovery of insight. Slow but continuous improvement and ultimate practical recovery, the hemianopic defect being the earliest to clear up and the disturbance of perception for movements and of position sense the last.*

L. T., a Negress aged 34, right handed, was referred to the neurologic service of Welfare Hospital on April 4, 1941. She had been admitted to the medical service on Dec. 10, 1940, with a three years' history of cardiac decompensation and hypertension, with a blood pressure of 210 systolic and 110 diastolic, and a 2 plus Wassermann reaction of the blood. The cardiac lesion was diagnosed as rheumatic heart disease.

On April 1, 1941 a peculiar feeling developed in the back of her neck, and shortly afterward she was unable to move her left arm and leg. Apparently there was a sudden, but not acute, apoplectiform onset without any material disturbance of consciousness. Her behavior then became peculiar. She did not realize, and on being questioned denied, that she was paralyzed on the left side of the body, did not recognize her left limbs as her own, ignored them as if they had not existed and entertained confabulatory and delusional ideas in regard to her left extremities, particularly her left arm. She said that another person was in bed with her, a little Negro girl, whose arm had been slipped into the patient's sleeve. She felt the supposedly foreign arm and leg as rather warm and heavy against her body, and, because the foreign limbs were never moved, she thought that her bedmate was constantly asleep. In an effort to awaken her, the arm was pinched and tossed about by the patient's right arm. She felt some pain but did not associate it with the pinching, being entirely unaware of the status of her left side. This situation continued for about five days, until another patient demonstrated the relationship of the left arm and leg to the owner's body and told her they were paralyzed. She then gradually regained appreciation of the fact that the imaginary arm and leg were her own extremities and recognized the nature of the accident and her illness, although a certain lack of insight into the unreality of the delusional experience persisted for some time.

Neurologic examination in the early period of observation revealed flaccid paralysis of the left side of the body, including the lower part of the face and the tongue. Left homonymous hemianopia was demonstrated grossly. Sensory disturbances on the left showed many thalamic-like qualities. There was hypesthesia for superficial sensation, with hyperpathia. There were diffusion and radiation of pain in pinprick, spontaneous pains, dysesthesias and paresthesias and difficulty in localizing and recognizing the nature of the noxious stimulus. Position sense and

perception of passive movements were lost. Stereognosis and two point discrimination were gone.

Improvement of hemiplegia (which after a short period of flaccidity became slightly spastic) proceeded relatively rapidly and led to almost complete recovery of motor power. Still sooner hemianopia disappeared. Sensory disturbances improved slowly but continually. First the hypesthesia receded, along with diminution of the hyperaffectivity, of the paresthesias and of the spontaneous pains, which gradually vanished. Localization, two point discrimination and stereognosis returned practically to normal, while position sense and perception of passive movements remained partially impaired in the fingers of the left hand for a long period, until they finally also were essentially restored.

The diagnostic impression was that of a thrombotic process in the right hemisphere, with particular involvement of the thalamoparietal radiation next to the cortex and/or the parietal region itself, especially the area of the supramarginal and angular gyri.

Three varieties of the syndrome under discussion can thus be observed. They may be classified as follows, according to their particular features: 1. Anosognosia, or lack of recognition of disease, with neglect of impressions from the paralyzed parts or side of the body and overlooking of hemiplegia. This may be (*a*) complete—in terms of total unawareness of disease—or (*b*) incomplete—in terms of ignorance of the nature of the disease, such as the paralysis and the accompanying sensory impairment, but with vague realization of some sort of disablement. 2. Anosognosia with amnesia for or imperception of the affected limbs or side of the body, in various degrees from simple forgetting or nonrecognition to obstinate denial of their existence. 3. Anosognosia which, in addition to the experience of absence, is associated with illusions or distortions concerning the perception of and confabulations or delusions referring to the affected limbs or side.

It is worth noting that practically all cases of lack of recognition or unawareness of cerebral hemiplegia so far reported have been those with involvement of the left side of the body in right-handed persons. This is in accordance with my own experience. In the literature there are cited some rare exceptions to this rule, namely, single instances of imperception concerning right hemiplegia. I myself have observed no case of this kind except in originally left-handed persons. The same is true of the cases in which not so much the defect as the defective parts or the entire left side of the body was forgotten or failed to be recognized as the patient's own to the extent of being experienced as absent, sometimes even without the presence of pronounced hemiplegia. It is also true of the cases in which illusions, confabulations, hallucinations or delusions relative to the disabled parts or side of the body were produced.

In the great majority of cases the hemiplegia was associated with homolateral loss of sensibility of different degrees, usually involving the epicritic and proprioceptive qualities more than the protopathic; the sensory disturbance was often thalamic in character or partook of the nature of it. Another frequent combination was the presence of more

or less decided impairment of perception in the left visual field, to the extent of left homonymous hemianopia. In a number of cases conjugate deviation of the head and eyes to the right side was noted. In some of them, however, the patient turned the whole body to the healthy side in a manner suggesting looking away from the nonappreciated or forgotten hemiplegic left side rather than genuine conjugate deviation (case of Kramer [14]; first case of Pötzl [7]; 1 of my cases).

PROBLEM OF VALUE OF THE SYNDROME IN CEREBRAL LOCALIZATION

The problem of value in cerebral localization of the phenomenon of imperception of somatic defect and its varieties has been the subject of study by a series of authors. Anton [4] expressed the opinion that the phenomenon was of value in cerebral localization. Babinski [5] also stated the belief that it had localizing significance. On the other hand, Redlich and Bonvicini,[15] in a study of the phenomenon of unawareness of cortical blindness, asserted that this condition was not of localizing value. They pointed out the peculiar psychic attitude of their patients, similar to that of the Korsakoff syndrome, for which reason they concluded the condition was a result of general impairment of cortical function rather than of a localized cerebral lesion. This concept, however, has not been substantiated by pathologic observations subsequently reported in the literature, especially those in cases showing the phenomenon of imperception of left hemiplegia, as well as the allied varieties. These observations have given full support to Anton's point of view.

Of particular interest in this connection are 2 cases studied by Pötzl [7] (1925) with the phenomenon of unawareness of left hemiplegia and delusions related to the left side of the body. In the first of these cases, in which the phenomenon persisted for several months, autopsy revealed a fresh hemorrhage adjacent to a cystic area in the right parietal lobe and a large area of softening in the right optic thalamus. In the second case, in which the phenomenon was likewise present for a considerable time, necropsy revealed a softening in the right parietal lobe and another softened area in the right optic thalamus. Pötzl assumed that it is the coincidence of lesions in the optic thalamus and the parietal lobe of the minor hemisphere on which the phenomenon is based.

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14. Kramer, F.: Alloaesthesie und fehlende Wahrnehmung der gelähmten Körperhälfte, Ztschr. f. d. ges. Neurol. u. Psychiat. **14**:58, 1917.

15. Redlich, E., and Bonvicini, G.: Ueber mangelnde Wahrnehmung (Autoanästhesie) der Blindheit bei cerebralen Erkrankungen, Neurol. Centralbl. **26**:945-951, 1907; Weitere klinische und anatomische Mitteilungen über das Fehlen der Wahrnehmungen der eigenen Blindheit bei Hirnkrankheiten, ibid. **30**:227 and 301, 1911.

In an earlier case, however, observed by Müller [16] (1905), in which the phenomenon was pronounced, autopsy showed a softening of the right supramarginal gyrus as well as a larger area of softening involving the anterior part of the internal capsule and the caudate and the lenticular nucleus on the right side and cutting posteriorly the right thalamocortical radiation, without affecting the thalamus itself. Moreover, in a report of a study on 5 cases of the syndrome under discussion, Pinéas [17] (1926) described 2 cases (clinically similar to Pötzl's cases) with autopsy, in 1 of which extensive softening occurred in the right hemisphere, affecting the supramarginal and angular gyri, as well as the insula, caudatum and putamen, with the optic thalamus intact; in the other case necropsy showed prominent softening in the area of the right central convolution, while both the right parietal lobe and the optic thalamus were macroscopically unaltered. Microscopic examination was not made. Pinéas also cited 2 cases reported by Anton [18] in 1893 from a different point of view, in which autopsy revealed a cortical softening extending from the posterior central gyrus to the occipital region.[19] Such cases seem to indicate that lesions of the area in the brain behind the posterior central gyrus in the minor hemisphere may be of sole or preponderant importance in causing the condition.

But Barkman [20] (1925), in reviewing the literature concerning the site of the lesion in cases of anosognosia with autopsy reports, showed that a lesion of the right thalamoparietal peduncle affecting the right optic thalamus produced the phenomenon. The conception of involvement of the right thalamus or the right thalamoparietal radiation in the cases in question received further confirmation through later reports.

In a series of 6 cases of the syndrome of anosognosia studied by Von Hagen and Ives,[21] autopsy in 1 (case 6) revealed an abscess involving the lateral and superior portion of the right optic thalamus and the adjacent thalamoparietal peduncle. This lesion was concluded to be responsible for bringing about the condition. In 2 other cases

16. Müller, F.: Ueber Störungen der Sensibilität bei Erkrankungen des Gehirns, in von Volkmann, R.: Sammlung klinische Vorträge, Leipzig, Breitkopf & Härtel, 1905, ser. 14, nos. 394-395.

17. Pinéas: Der Mangel an Krankheitsbewusstsein und seine Variationen als Symptom organischer Erkrankungen, Verhandl. d. Gesellsch. deutsch. Nervenärzte **16**:238-248, 1926.

18. Anton, G.: Beiträge zur klinischen Beurteilung und zur Lokalisation der Muskelsinnstörungen im Grosshirne, Ztschr. f. Heilk. **14**:313-348, 1893.

19. A lesion of the cuneus, gyrus cinguli and calcar avis was included in the softening.

20. Barkman, A.: De l'anosognosie dans l'hémiplégie cérébrale; contribution clinique à l'étude de ce symptôme, Acta med. Scandinav. **62**:213-254, 1925.

21. Von Hagen, K., and Ives, E. R.: Anosognosia (Babinski), Imperception of Hemiplegia: Report of Six Cases, One with Autopsy, Bull. Los Angeles Neurol. Soc. **2**:95-103, 1937.

with the clinical manifestations of the syndrome reported by these two authors [22] autopsy demonstrated a lesion not affecting the thalamus itself, but so situated as to cut off the connections between the right thalamus and the cortex and to separate them from one another. In the first of these cases (with left hemiplegia, sensory impairment and hemianopia on the left side) there was a large hemorrhage into the right corpus striatum just lateral to the right optic thalamus, which itself presented no evidence of any significant lesion. In the second case (with left hemiplegia and impairment of sensation) section of the brain showed softening and edema of the right parietal lobe, including the supramarginal and angular gyri and the inferior portion of the superior parietal lobule, the lesion involving the white matter down to the region of the corona radiata but not the optic thalamus. It is apparent from these instances that a lesion in the immediate vicinity of the optic thalamus in the minor hemisphere may lead to the phenomenon of anosognosia, as does a lesion of the thalamus itself; this is probably due to isolation of the latter from the cortex, particularly from that of the parietal lobe.

Of 2 cases of anosognosia with amnesia and delusions concerning the paralyzed left limbs reported by Ives and Nielsen,[9] postmortem study disclosed in 1 a small lesion in the right hemisphere affecting the retrolenticular part of the internal capsule and to some extent the thalamus, and also softening the thalamoparietal peduncle. In the other case there was an extensive area of softening in the right parietal lobe, including the supramarginal and angular gyri.

Nielsen [23] reported 5 other verified cases of the phenomena in question, in all of which the right thalamoparietal peduncle was involved. In the first case, with forgetting of the left side of the body, autopsy showed a large deep neuroglioblastoma multiforme in the right parietal region, with involvement of the thalamoparietal radiation. In the second case, with amnesia for the left limbs and left hemianopia, necropsy revealed an area of softening in the right parietal region, destroying the supramarginal gyrus and undermining the angular gyrus; it extended down to the splenium corporis callosi. In the third case, with unawareness of the left limbs, autopsy revealed a hemorrhagic area in the right external capsule, extending from the anterior border of the insula to the pulvinar of the thalamus. In the fourth case, with denial of the presence of the left limbs, necropsy disclosed a softening in the area of distribution of the right middle cerebral artery, with sparing of the thalamus. In the fifth case, with thrombosis of the terminal branches of the right middle

22. Von Hagen, K., and Ives, E. R.: Two Autopsied Cases of Anosognosia, Bull. Los Angeles Neurol. Soc. **4**:41-44, 1939.

23. Nielsen, J. M.: Disturbances of the Body Scheme: Their Physiological Mechanism, Bull. Los Angeles Neurol. Soc. **3**:127-135, 1938.

cerebral artery and with delusions concerning the left, paralyzed arm, section of the brain demonstrated softening in the right hemisphere, evidently affecting the thalamoparietal peduncle.

While it cannot be denied that divergencies in the relative changes observed at autopsy still exist, there is, on the other hand, increasing evidence that the condition is most likely to result from lesions affecting the right optic thalamus or right thalamoparietal radiation or the parietal cortex in the minor hemisphere. Moreover, the fact seems to emerge that lesions nearer to or within the structure last mentioned, particularly lesions of the cortex about or below the right interparietal fissure, are more apt to induce the psychologically complex manifestations of the condition than those farther away from it, or closer to the thalamus, which may or may not be immediately involved. Yet the problem of the localizing value of the syndrome needs clarification through further study, especially in view of the fact that it is a specific form of psychic disturbance produced by a local cerebral lesion.

PHYSIOPSYCHOLOGIC ASPECT OF THE CONDITION

There are, consequently, three factors which deserve consideration: first, the site and mode of onset of the structural lesion; second, the particular physiologic disturbance it evokes, and, last, the nature of the psychologic manifestations of the condition.

I believe there can be no doubt that the specific form of psychic disorder presented by the cases in question is the result of a local lesion in the brain. The site of the lesion can already be indicated with a reasonable degree of probability, though its exact topographic relation has not yet been definitely established. It seems, however, that the cortex surrounding the interparietal sulcus, especially the region in the lower part of the parietal lobe, in the minor hemisphere represents the main junction in the functional chain of the process.[24] The specific physiologic involvement, secondary to the lesion, evidently takes place on a higher level of neural integration, namely, one concerned in the mechanism of body orientation. The physiologic disturbance of that mechanism, reflecting into the psychic sphere in a particular manner, in turn evokes an equivalent disturbance in a specific psychic activity. Yet it does not necessarily entail lowering or impairment of general cortical or mental function. Indeed, the patients are not as a rule demented; their sensorium, orientation, memory, attention and judgment

24. As will be shown later, this process extends physiologically from the parietal cortex of the major hemisphere to the periphery of the body, the relation to the right side of the body being direct and that to the left side being indirect, i. e., by way of the interhemispheral connections with the minor parietal cortex as the focal point.

are good except for the amnestic-agnostic disturbance in the sphere of body awareness and recognition; in other words, the activity of the mind as a whole is uninterrupted.

Thus, the local cerebral lesion involving a specific physiologic mechanism causes a certain group of experiences in the field of body consciousness, or some corresponding specific form of psychic activity, to be blocked off from general consciousness. This abolition may be of temporary or lasting nature, probably dependent on the site and the extent of the lesion and, also, on the mental attitude of the patient. The specific psychic disturbance can fairly be defined as a dissociation from interest, attention, memory and cognitive appreciation of a certain defect in somatic function or of a defective section in the somatic sphere. It manifests itself in the patient's consciousness as an isolated negative state, that is, as absence of disease or of the disabled parts or side of the body. To the patient the affected limbs or side either does not seem to be paralyzed or impaired in sensation or changed at all,[25] or simply ceases to exist. This negative state in the patient's conscious experience gives rise to the appearance of positive psychopathologic features, such as confabulations, delusions and illusions, related to parts of the body split off from awareness at the time. With recovery from the condition, the presence of disease or of the nonrecognized parts of the body returns to consciousness, and the patient then realizes the abnormal situation and complains of it.

CONCEPT OF BODY SCHEME

The question now arises: What is the basic physiologic principle underlying the condition under discussion? It is true that in a large majority of cases of this disturbance there is concomitant loss of sensibility, indicating serious impairment of the sensory apparatus. This may play a certain part in the activation of the phenomena. It cannot, however, explain in any way the disorder in body orientation or body consciousness apparent in the condition. Beyond the sensory apparatus

25. Attempts have been made, particularly by Schilder (The Image and Appearance of the Human Body, London, Kegan Paul, Trench, Trubner & Co., 1935) and by some other authors, to explain psychologically the condition of unawareness of disease and its varieties on the basis of the assumption of a determining tendency or a primary instinctive urge toward maintenance of the integrity of the body, governing the patient's behavior. According to this theory, there obtains here a certain type of repression, similar to the so-called purely psychic one, but based on an organic mechanism in the cases in question. Schilder spoke of an organic repression. This interesting hypothesis seems to me unsatisfactory, for it fails in the face of the essential fact that it is mainly, if not exclusively, in cases of left hemiplegia of right-handed persons that the syndrome usually occurs. It would be surprising, indeed, if the inherent instinctive urge toward maintaining the integrity of the body should operate in cases of hemiplegia of the minor and not in those of the dominant side.

there is no doubt a more complex specific physiologic mechanism involved, chiefly represented in the parietal region of the dominant cerebral hemisphere, the integrity of which is essential to the normal functioning of recognition of and orientation as to the body. This mechanism can be interfered with both directly, i. e., by lesions in the dominant hemisphere, and indirectly, i. e., by lesions in the minor hemisphere.

I believe that the syndrome of unawareness of disease (hemiplegia or other defect) or of imperception of defective parts or side of the body can best be interpreted on the basis of the concept of the so-called body scheme, or body image, or postural model of the body, as have been the direct agnostic disturbances in body orientation.

This concept, which is concerned with body consciousness and its disorders, can largely be attributed to Pick,[26] Head[27] and Schilder.[28] It has, however, not attracted much attention among neuropsychiatric workers for many years. This is apparent from the relative scarcity of adequate studies on the subject. It was not until recent years that the concept of body consciousness, or body scheme, gained increasing interest in some neurologic and psychiatric circles.

By body scheme, or body image, is understood the inner picture or model which one forms in one's mind of one's body or one's material self, in the course of life, and which one carries with one unwittingly, that is, outside of central consciousness. It is a kind of inner diagram representing one's body as a whole, as well as its single parts according to their location, shape, size, structural and functional differentiation and spatial interrelation. It also represents the cardinal directions of the body—right and left, anterior and posterior, up and down. The body scheme can thus be conceived of as a complex of intimately correlated individual schemas; some of them seem to predominate over the rest. There is conclusive evidence, on the basis of specific investigations, that tactile, kinesthetic and optic experiences, and probably to a minor degree other receptive factors, contribute in the integration of the body scheme to a highly organized arrangement, in the service of orientation and recognition in the body sphere and, in a broader sense, of the relation of the body to external objects and space. Like all highly integrated neural arrangements, this is a process of physiopsychic activity. The specific psychic nature of the body scheme is essential in determining the forms assumed by the manifestations resulting from its disorders.

26. Pick, A.: Ueber Störungen der Orientierung am eigenen Körper, in Arbeiten aus der psychiatrischen Klinik in Prag, Berlin, 1908; Zur Pathologie des Bewusstseins vom eigenen Körper, Neurol. Centralbl. **34**:257-365, 1915.

27. Head, H., and Holmes, G.: Sensory Disturbance from Cerebral Lesions, Brain **34**:102-254, 1911. Head, H., and others: Studies in Neurology, London, Oxford University Press, 1920, vol. 2.

28. Schilder, P.: The Image and Appearance of the Human Body, Psyche Monographs, London, Kegan Paul, Trench, Trubner & Co., 1935, no. 4.

AFFERENT IMPRESSIONS AND BODY IMAGE

The body scheme is to be thought of not as something that is static, but in terms of a dynamic process that constantly repatterns itself under the continuous stream of influences exerted through the ever varying afferent impulses. One's orientation in the body sphere depends, on the one hand, on the normal functioning of the specific central apparatus subserving the body image and, on the other hand, on the fact that every impression or perception evoked by postural, spatial or other change in one's body is being recorded in a constructive manner on the plastic body schema. Every new set of afferent impulses, in order to serve the body orientation, must be brought into proper functional relation with the mechanism of the body image by the activity of the brain before they rise into consciousness. This relation gives them the intimacy characteristic of all experiences which one appropriates as one's own. Without that relation the peripheral impression results in an isolated perception accompanied by a feeling of estrangement and separation from the body. It is the relation between sensory impressions and body image also that determines their definite elaboration and gives them their final significance. The act of recognition of a bodily alteration, of whatever nature, is effected if the sensory impulses entering into awareness are charged with a complete relation to the physiologic and psychologic dispositions of the body schema, a relation going on at unconscious levels, but reflecting into the sphere of conscious cognition.

The sequence of events necessary for the ordinary relation between sensory receptions and the postural model of the body may be disturbed or interrupted, first, if the body scheme proper is thrown into disorder and, second, if there is a breach at a connective link in the functional chain between the cortex and the periphery of the body. The former may occur in consequence of a correspondingly located lesion in the major (left) cerebral hemisphere, involving the chief representation of the body schema in the parietal or parieto-occipital region. The latter may be brought about by a lesion in the minor hemisphere blocking or interfering with the correlated commissural and associational formations. Either type of lesion will result in some specific form of loss of recognition and orientation in the body sphere.

DIRECT DISORDERS IN THE BODY SCHEME

In cases of the first type the lesion will produce the condition of agnosia within the range of the somatic self and its constituents, a somatotopagnosia, as it were—that is, a primary disturbance or loss of ability for recognition of and orientation as to the various parts of the body (one's own as well as that of others) and their spatial interrelation, without the patient's becoming aware of the disorder spontaneously.

Pick [29] called this condition autotopagnosia. A patient suffering from a disorder of this type cannot differentiate or indicate the individual parts of the body on command, is helpless when asked to point specifically to the chin, mouth, eyes, ears, shoulders, etc., and commits striking errors in appropriate tests. Furthermore, the patient may show disturbance or loss of ability for recognition and orientation as to right and left and other directions in his own body, and also in that of other persons. The capacity, however, for recognition and orientation in external space and with respect to objects outside the body, the so-called allognosis, or object gnosis, is, in my experience, practically unimpaired, at least in typical cases. It has been demonstrated by Pick and others that these disorders are due to lesions of the parietal lobe. Unfortunately, in most cases of the disturbance the local lesion is accompanied by a more or less diffuse cerebral process. This is why clearcut instances of so-called autotopagnosia [30] are only rarely, if ever, encountered, even if one searches a long time for them, as I did for many years. The coincidence in cases of autotopagnosia of local and more expansive, particularly more diffuse, cerebral lesions usually results in psychic disturbances, in aphasic, apractic and other agnostic manifestations, behind which disturbances of recognition and orientation in the body sphere for the most part are hardly discernible, or not at all.

The scarcity of typical cases of autotopagnosia in the literature warrants a brief report of an instructive case of this kind which I have recently observed.

CASE 3.—*History of hypertension for the past few years and of a positive Wassermann reaction of the blood. Two cerebral vascular accidents at an interval of about three months, the first resulting in right hemiplegia and verbal aphasia, from both of which the patient apparently recovered, and the second being followed by recurrence of the right hemiplegia but no aphasia. Initial impairment of memory, especially for recent events, with subsequent improvement. Present symptoms: Right spastic hemiparesis; no anosognosia; generalized autotopagnosia, predominantly with regard to paired organs; disorientation as to laterality, with the peculiar feature of persistent mutual transposition of right and left, on the body; partial finger agnosia; complete agraphia, but retained ability of reading; marked acalculia, with a peculiar type of arithmetical dissociation; no constructive apraxia; no aphasia, except for amnesic difficulty in word finding; incomplete amnestic color blindness, with slight uncertainty in color recognition; no visual agnosia for objects, pictures, external space, geometric figures, etc.; no hemianopsia.*

A. R., a white woman aged 70, single, a nurse, was admitted to the medical service of the First Division, Welfare Hospital, on Oct. 23, 1941 from New York Post-Graduate Hospital, with complaints of paralysis on the right side and partial

29. Pick, A.: Störung der Orientierung am eigenen Körper, Psychol. Forsch. **1**:303-318, 1922.

30. I believe somatotopagnosia might be a more appropriate term, since in cases of this type the disorientation and loss of recognition concern not only the patient's own body but usually also that of other persons.

loss of speech since June 1941 and hypertension for the past few years. On June 21, 1941, on arising, the patient noted that she was unable to move her legs from the knees down. She remained in bed, but that night became suddenly unconscious for several hours, after which she was unable to speak or move her right side. During the next few months speech and motor power on the right side improved significantly, so that she could move her right extremities again and speak in a normal manner (according to a report by a friend). Three months later, in September 1941, she suffered another "setback," during which she "went limp" and was totally blind for half an hour; after this her right side was again completely paralyzed. Shortly thereafter (September 29) she entered the Post-Graduate Hospital, where some improvement in movements of the right arm and notable improvement in speech were noted. A 4 plus Wassermann reaction was found on routine examination. The patient was seen in consultation with members of the division of neurology on October 16, to which she was then transferred.

Physical examination on admission revealed normal pupillary reflexes, arteriosclerosis of the peripheral and fundal arteries, slight enlargement of the heart and a blood pressure of 160 systolic and 86 diastolic. A 4 plus Wassermann reaction of the blood was reported on October 27. Examination of the spinal fluid revealed no abnormalities.

Examination of the eyes shortly after admission showed vision to be 10/200 in the right eye and 10/400 in the left eye. The fundi showed thinned and tortuous veins, a few hemorrhagic areas and patches of exudate in the left eye. There was slight cupping of the disks. Reexamination by an ophthalmologist in consultation on November 17 revealed vision to be 20/100 in each eye.

Examination at the neurological service, Welfare Hospital, revealed the following changes: 1. Disturbance in memory, particularly for recent events, with secondary disorientation as to time and place. This improved greatly in the course of about two weeks, temporal and spatial orientation returning practically to normal, but some difficulty in retention and recall remained. 2. Right spastic hemiplegia with weakness of the right lower part of the face and deviation of the tongue to the right. No material disturbance of sensibility was noted. 3. Amnesic aphasia of relatively slight degree, consisting essentially of a certain difficulty in finding names and in recalling more unusual words, with no disturbance in any other aspect of speech. Understanding of speech was normal. 4. Disability in finding the names of certain colors, particularly green, and in recalling them, and frequently also in recognizing them by name, while being able to match colors properly except for occasional slight errors. The condition resembled the amnestic color blindness of Wildbrand. 5. Practically complete agraphia both for words and numbers, and even letters and digits, with inability to write spontaneously, to dictation and to copy with the left, nonparalyzed hand. 6. Relatively preserved ability to read, which was first difficult to evaluate because of poor vision. After some improvement of vision, she was able to spell and read correctly, provided printed or written matter was presented with words and letters large enough for her to see. 7. Impairment in calculation, with practically complete inability to add, subtract or divide, while the ability to multiply was preserved to a striking degree.[31] 8. Disability in recognition

31. A sample from my record may illustrate this striking arithmetical dissociation: When the patient was asked "How much is 6 + 5?" she repeated "6 and 5 to it," and said: "I don't know; I can't even make a guess." On being asked "6 — 3 = ?," she declared: "There is no such thing." [Why not?] "Because it

of and orientation as to the various parts of the body in terms of autotopagnosia. This was particularly noticeable for the paired organs and was more pronounced in those of the face than in the rest of the body. Responses were variable. 9. Partial finger agnosia, particularly involving the three middle fingers of both hands. 10. Disorientation as to right and left of the body, with regular confusion of the right side for the left and vice versa—a peculiar feature, which presented itself in terms of transposition or inversion of laterality.

A few observational data from my records concerning the phenomena listed under items 8, 9 and 10 may be presented here.[32] When requested to point to or grasp a part of the body, the patient sometimes succeeded in doing so. At other times, however, she was quite helpless and responded in a striking manner, although she understood perfectly and repeated correctly whatever task she was to perform. For example, when asked to grasp her right or her left ear, she would try eagerly, but without success, and then behave in an increasingly confused fashion. In spite of a normal sensorium and her appreciation of what she was being asked for, she would look around the bed as if seeking something, stare at the examiner and say, "I don't have them; my ears must have been cut off and thrown away." On being questioned, she would declare: "They were no good, I guess; they were paralyzed." On repetition of the request, she would point to the wrong ear, i. e., to her left ear for her right, or vice versa, or grasp another part of her face, or she would again become confused and give up. Similarly, she frequently failed in finding her right or left eye and behaved in the same way. On one occasion, when asked to point to her eyes, she said: "There, there . . ." Asked "where?," she stated: "I don't know. I thought that would be easy to find. I haven't got any." Her orientation was likewise poor with regard to other parts of the body, such as the nostrils, cheeks, shoulders and elbows. Asked, for instance, to lift her left arm, she said: "I can't, it is paralyzed." When her attention was directed to the fact that this arm was normal, she declared: "I guess it isn't." On another occasion, to the question, "Where is your left arm?" she answered "I don't know; for God's sake, it must have been cut off and thrown away." Asked why, she said: "Because it was in the way." Asked to point to her lower limbs, which were covered with the blanket, she tried to find them above the cover, and then said in a helpless way: "You got me again. I don't know; I must have lost them. Perhaps they cut them off because they were of no use." Orientation for the nonpaired parts of the face and the rest of the body was comparatively less affected. In respect to the bodies of other persons, the patient's disturbance in recognition and orientation was of lesser degree than that for her own body, but errors of similar nature were produced in the appropriate tests.

The patient's disorientation for the right and the left side of the body manifested itself in a particular way; that is, there was not merely a disturbance in recognition of laterality with respect to herself, as well as to the examiner, but she also showed a constant tendency toward inversion of the sidedness of paired organs by putting

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couldn't be, wouldn't be possible." ["What did I ask you?"] "6 — 3; it isn't possible, absolutely not. You can't take away 3 from 6; I know what I am talking about and you can't fool me either." When told that the result is 3, she said: "I guess so; I guess it is." Presented with the problem $8 \div 2$, she remarked: "There is no such crazy number like that; you get me all twisted up." ["What did I ask you?"] "8 divided by 2; I don't know it; honestly, I don't." But if given multiplication problems, such as 6×5, 3×9, 4×8, and the like, answers were prompt and correct.

32. The other phenomena will be discussed in more detail in another article.

each side in the place of the other. She persistently confused her right extremities, especially the arm and hand, for her left, and vice versa. On questioning, she declared that the left side was the hemiplegic one and the right was intact, at the same time pointing to the paralyzed side as being the left and to the nonparalyzed side as being the right, without awareness of her errors. Also, the sides of those organs which were not included in the hemiplegic condition, such as the ears and eyes, were mutually transposed by her. In tests in which she did succeed in finding the part of the body she was asked for, she nevertheless regularly erred as to the side, pointing to the left for the right and vice versa. Every attempt at making her realize her error was of no avail and resulted only in her becoming more confused. The disturbance of the capacity for recognition and of orientation as to right and left was essentially confined to the body sphere; that is, it did not apply to the ability to distinguish right from left in space and with respect to objects outside the body.

Whereas a notable improvement in the autotopagnosia of the patient could be demonstrated after several weeks of observation, there was no tendency for her right-left disorientation to improve. As the general disorientation in the body sphere subsided, there became more pronounced a circumscribed disturbance of orientation involving specifically the fingers of either hand, it formerly being in the background, as though concealed by the general body disorientation. The disturbance manifested itself in the following ways: The patient failed on request to recognize, select, name and demonstrate single fingers on her own hand, as well as those on the examiner's hand. The disorder appeared in variable degrees and was more noticeable in the middle three fingers than in the outer fingers. While this disability was more often demonstrable in tests involving distinction between right and left, it showed itself irrespective of whether or not laterality was simultaneously tested. It seemed, however, that the peculiar impairment of appreciation of right and left rendered the tests for finger gnostic performance particularly difficult for the patient.

The diagnostic impression was that of an older (reversible?) vascular lesion in Broca's area and the left precentral region and a recent softening in the left lower parietal or parieto-occipital region.

The only clearcut instance of disorder of the body image proper so far presented is the syndrome of finger agnosia.[33] As has generally been

33. Gerstmann, J.: Fingeragnosie. Eine umschriebene Störung der Orientierung am eigenen Körper, Wien. klin. Wchnschr. **37**:1010-1012, 1924; Fingeragnosie und isolierte Agraphie, ein neues Syndrom, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:152-177, 1927; Zur Symptomatologie der Hirnläsionen im Uebergangsgebiet der unteren Parietal- und mitteleren Occipitalwindung, Nervenarzt **3**:691-695, 1930; Syndrome of Finger Agnosia, Disorientation for Right and Left, Agraphia and Acalculia: Local Diagnostic Value, Arch. Neurol. & Psychiat. **44**:398-408 (Aug.) 1940. Hermann, G., and Pötzl, O.: Ueber die Agraphie und ihre lokaldiagnostischen Beziehungen, Berlin, S. Karger, 1926. Lange, J.: Fingeragnosie und Agraphie (eine psychopathologische Studie), Monatschr. f. Psychiat. u. Neurol. **76**:129-188, 1930; Agnosien und Apraxien, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 6, pp. 807-957. Schilder, P.: Fingeragnosie, Fingerapraxie, Fingeraphasie, Nervenarzt **4**:625-629, 1931; Localization of the Body Image (Postural Model of the Body), A. Research Nerv. & Ment. Dis., Proc. **13**:466-484, 1932. Klein, R.: Ueber die Funktionen des Parietallappens, Nervenarzt **6**:1 and 67, 1933. von Stockert, F. G.:

confirmed, this condition consists in a primary selective disturbance or loss of ability to recognize, identify, differentiate, name, select and indicate the individual fingers of either hand, the patient's own, as well as those of other persons. It is characteristically associated with disorientation for right and left in respect to the patient's own body, as well as that of other persons, with special reference to the hands and fingers. These symptoms are commonly combined with an isolated disturbance of writing—agraphia—and an isolated disability for calculation—acalculia—of differing intensities and definite character. Investigations in a large number of cases of this type have so far failed to reveal any evidence of psychic, particularly of intellectual, disorder, of aphasia, apraxia or other manifestations of agnosia or of motor or sensory changes to which the symptom complex of finger agnosia or its individual features could be related. The condition of finger agnosia occurs in spite of the patient's adequate theoretic knowledge of the hands and fingers, in spite of the absence of disturbance of general optic and tactile comprehension, in spite of sufficient vision to guide him and, last but not least, in spite of normal sensibility. It is noteworthy that mistakes with regard to the three middle fingers are usually more pronounced than those relating to the thumb and the little finger. The patient as a rule does not become aware of his errors spontaneously and is quite helpless in controlling them.

Finger agnosia may thus be defined as a circumscribed disturbance of the capacity for recognition and orientation in one section of the body. As far as the limbs (including the toes) and the other parts of the body are concerned, ability to recognize them and to orient with reference to them remains essentially unaltered.[34] It is as though in finger agnosia the body scheme were affected in one sphere only, and, indeed, in the most significant, differentiated and vulnerable one—the sphere corresponding to the individual fingers—as though the optic-tactile-kinesthetic image appertaining to the fingers were split off from the total

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Das Gerstmannsche Syndrom der Fingeragnosie, mit besonderer Berücksichtigung der Sprach- und Schreib-Störung., Monatschr. f. Psychiat. u. Neurol. **88**:121-151, 1934. Mussio-Fournier, J. C., and Rawak, F.: Glioblastome de l'hémisphère gauche avec syndrome de Gerstmann: Réaction mélanophorotrope sur la grenouille par l'urine de la malade, Rev. neurol. **2**:681-685, 1934. Muncie, W.: Finger-Agnosia (Gerstmann), Bull. Johns Hopkins Hosp. **57**:330-342, 1935. Mayer-Gross, W.: Some Observations on Apraxia, Proc. Roy. Soc. Med. **28**:66-72, 1935. von Angyal, L.: Beiträge zur Symptomatologie, Lokalisation und hirnpathologische Auffassung des Gerstmannschen Syndroms, Ztschr. f. d. ges. Neurol. u. Psychiat. **156**:245-264, 1936. Strauss, A., and Werner, H.: Deficiency in the Finger Schema in Relation to Arithmetic Disability (Finger Agnosia and Acalculia), Am. J. Orthopsychiat. **8**:719-725, 1938; Finger Agnosia in Children, Am. J. Psychiat. **95**:1215-1225, 1939. Nielsen.[8]

34. Brain, R. W.: Visual Object-Agnosia with Special Reference to the Gestalt Theory, Brain **64**:43-62, 1941.

body image, the finger scheme from the total body scheme. Finger agnosia with disorientation for right and left, agraphia and acalculia, usually caused by a local process affecting the lower part of the parietal lobe, or specifically the angular gyrus in its transition to the second occipital convolution, seems to be the only disturbance of the body scheme proper which can be found as a result of a focal cerebral lesion.

In contrast to the scarcity of reports on cases of autotopagnosia in the literature, reports on finger agnosia and the associated features are numerous. In fact, there exists a considerable number of careful studies on the syndrome made by various authors,[35] from which extensive mutual confirmation of the data on finger agnosia and the accompanying symptoms is apparent. For this reason, as well as for that of limited space, I shall abstain from reporting the interesting cases of 2 patients with the syndrome of finger agnosia whom I have recently examined,[36] 1 with a left-sided cerebral tumor verified by biopsy, and the other[37] supposedly with two thrombotic lesions in the left precentral and Broca's area and in the left parieto-occipital transitional region, respectively.

INDIRECT DISORDERS OF THE BODY SCHEME

In cases of the second type apparently the postural model of the body is not directly, but is indirectly, involved. Speaking pathophysiologically, it is not the area of central representation of the body scheme, i. e., the parietal region in the major (left) hemisphere, that is affected by the lesion in this type. The lesion of the parietal area in the minor (right) hemisphere or of the right thalamoparietal peduncle or of the right thalamus itself, blocking (through shock, pressure or edema) or interfering with commissural and associational formations, and thus isolating the right hemisphere from the left, appears to be the essential factor here. The disturbance in the physiologic correlation of the two hemispheres is the intervening link between the morphologic change and the clinical manifestations. Gradually an adjustment may take place, and the condition in question is then abolished. This has been the outcome in a large majority of instances. If, however, the interrupting effect of the lesion on the specific physiologic correlation between the subordinate and the parietal mechanism in the dominant hemisphere does not reverse, the condition will persist for a considerable time, even until death.

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35. In this country special studies have been made by Schilder, Muncie, Nielsen and other members of the Los Angeles neurologic school and by Strauss and Werner.

36. One at the Neurological Institute and the other in the neurologic service, First Division, Welfare Hospital.

37. This patient has manifested two clinical conditions: an older, right hemiparesis with partial expressive aphasia of the motor type, and an apparently later syndrome of finger agnosia, right-left disorientation, etc.

Under disturbances of this type are included (1) cases of imperception of disease or defect in function (*a*) complete or (*b*) incomplete (cerebral hemiplegia with impairment of sensation on the minor side, cortical blindness, cortical deafness, certain forms of aphasic disorder, fantom limb, and the like); (2) cases of imperception of the defective parts or side of the body, with forgetting of their existence or nonrecognition of their possession, and (3) cases in which with the experience of absence of the affected limbs or side of the body are associated illusional, confabulatory or delusional ideas of a peculiar nature.

The syndrome of unawareness of (left) hemiplegia has been termed by Babinski anosognosia. This term, though established in the literature merely for hemiplegia, is likewise applicable to nonrealization of defects other than hemiplegia, such as cortical blindness. The syndromes of imperception of and psychotic elaboration with respect to the defective limbs or side of the body (sometimes even without hemiplegia's being present) for which the same term has hitherto been in use, need, in my opinion, a more accurate designation, for reasons already mentioned. The conditions featuring the cases of the second group I propose to call autosomatamnesia and autosomatagnosia, respectively, the former connoting dissociation from memory and the latter dissociation from conscious recognition of individual defective parts or the entire side of the body.[38] For the condition predominating in cases of the third group, I believe the designation somatoparaphrenia to be suitable, since it takes account of the fact that in the negative state of experience of absence of a certain part or area of the body, induced by disease, positive psychopathologic phenomena in the sphere of the body scheme are apt to occur. These terms seem to me to be more appropriate in describing the conditions concerned as they actually present themselves and in properly separating them from the mere condition of anosognosia, or lack of knowledge for disease.

This group of conditions arising from indirect pathophysiologic disturbance of the body image differs clinically in various respects from the group of disorders in body orientation resulting from direct involvement of the body scheme, which has been discussed before. The conditions here are characterized, first, by the association with a somatic defect in the periphery, affecting a certain portion of the body or complex of bodily activities; then, by the limitation of the phenomena referable to the body scheme to the diseased areas of the body in the majority, if not in all, of the cases; by the retained orientation with regard to the body of other persons, as well as to the rest of the patient's own body; by the frequent lack or difference in type of disorientation as to laterality, and, finally, by a specific form of behavior.

38. In a given case one might speak of monosomatamnesia or hemisomatamnesia and of monosomatagnosia or hemisomatagnosia, respectively.

THE FANTOM LIMB AND BODY SCHEME

Among the disorders illustrating the concept of the body image and its existence, as well as its relation to the body surface, the so-called fantom limb occupies a special position. As has commonly been recognized since the observations of Ambroise Paré, and particularly of Weir Mitchell,[39] this phenomenon may develop in persons who have suffered loss of an arm or a leg or parts of the limb. There have also been mentioned in the literature cases of fantom after amputation of other sections of the body, for example the breast or phallus. Apparently, a sudden loss is essential for the occurrence of the fantom.[40] The fantom may persist, in a variable degree, for a period of more or less length after the amputation. It is particularly vivid immediately after the operation. The patient may be possessed by the fantom to such an extent as to forget the defect entirely, as well as the fact of amputation.

The experience of further existence of the lost limb undergoes changes in the course of time. The fantom limb, which first corresponds in shape and size to the amputated extremity, gradually changes and becomes shorter. If the arm was involved, it is reduced little by little in the fantom; the hand approaches the stump or remains in the previous position, the intermediate parts disappearing; it may also become smaller, like that of a child. The same is, in the main, true of the leg.[41] The longer persistence of the hand and foot in the fantom gives evidence that the representation of these parts of the limbs in the body scheme differs in stability from that of other sections; this is not surprising in view of the difference in their physiologic importance and differentiation.

Not infrequently the position in which the patient lost his extremity is preserved in the fantom. It is as though the last posture of the limb was recorded on the body scheme.

In some patients the fantom limb is motionless; in others, however, it is believed to move spontaneously or to be movable at will. Movements of the healthy limb or parts of it are apt to produce the experience of similar or identical movements in corresponding parts of the fantom limb. This sensation of contralateral symmetric associated movements

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39. Mitchell, S. W.: Injuries of Nerves and Their Consequences, Philadelphia, J. B. Lippincott & Co., 1872.

40. The fantom usually does not occur in cases of slowly developing bodily losses. The suddenness in the occurrence of the defect is common to cases both of the peripheral and of the cerebral types of imperception.

41. I have recently observed a patient at the First Division of Welfare Hospital who had lost his left leg about twenty-five years ago, after a complicated fracture which necessitated amputation through the upper third of the leg. He has perceived a fantom limb ever since, which first corresponded in shape and size to the original part and then gradually became reduced to the foot and toes only; the latter, however, have remained in their previous position, while the intermediate part of the leg has vanished.

can be interpreted in terms of transmission of the cortical intention and formula of movement from the normal to the fantom side.

There are some reports in the literature suggesting that a fantom may also occur when the limb is not lost but is severely affected in function, for example, after laceration of nerves of the brachial plexus or after a transverse lesion of the spinal cord (Mayer-Gross [42]). However, the fantom of a disabled, but existent, part of the body seems to differ in some respect from that substituting for an absent one.[43]

In persons who have had amputation of a limb in earliest childhood or whose loss has been congenital, fantom phenomena are lacking, according to A. Pick. This is not surprising, because in such persons the body scheme has been built up to the exclusion of the originally missing part; in other words, the amputated part has never come to be represented in the body image.

The fantom phenomenon ranks somewhat differently among the various manifestations of body disorientation discussed in the preceding paragraphs. First, it occurs without any structural change in the brain. Interestingly, in a case reported by Head the fantom limb disappeared after a localized cortical lesion of the brain.[44] Second, it deviates from the cerebral type of imperception of somatic defect so far as with the fantom limb one is dealing with nonrealization of the actual absence of a certain section of the body, while in the cerebral type of imperception the condition of unawareness concerns existent, though functionally defi-

42. Mayer-Gross, W.: Ein Fall von Phantomarm nach Plexuszerreissung, Nervenarzt **2**:65-72, 1929.

43. A particularly interesting illustration of the principles of the body scheme is presented by a case of Head, which may be cited here. His patient had received a gunshot injury, which had disorganized the elbow joint and completely destroyed the ulnar nerve. For five months it was hoped that it would be possible to save the patient's limb, but at last it had been amputated, through the lower third of the arm. Head wrote (Aphasia and Kindred Disorders of Speech, New York, The Macmillan Company, 1926, vol. 1): "From the time he [the patient] was wounded, there were the usual changes, both motor and sensory, associated with complete ulnar paralysis; but the little finger alone was devoid of all forms of sensibility, superficial and deep. So long as he retained his limb, this finger seemed to him a dead object attached to the hand. But the phantom hand, which appeared after amputation, had four digits only. During the five months of total insensibility, the scheme associated with the little finger, no longer reinforced from the periphery, had gradually died away, and when the actual hand was removed, this digit was absent from consciousness. A portion of the body, cut off from the central nervous system, but attached to structures endowed with sensibility and movement, may continue to exist as a 'dead' part of ourselves; it occupies a certain place in our special activities. But as soon as the structures on which it is based are removed, it disappears from consciousness, whilst the normal parts of the amputated limb are represented in phantom form."

44. Unfortunately, I was unable to find a detailed report of this case in the literature.

cient, body territories. Nevertheless, the complex central mechanism engaged in the process is essentially the same in both the fantom and the cerebral type of imperception. In the explanation of either the main emphasis must be placed on the body scheme.

SUMMARY AND CONCLUSIONS

The problem of the phenomena of imperception of disease and of the related types of amnesia for or nonrecognition of or consecutive psychotic production with respect to the impaired parts or side of the body is studied. The anatomic, physiologic, psychologic and clinical aspects of the subject are discussed. The question of the value of the phenomena in cerebral localization is also alluded to. The concept of the so-called body scheme and the relation of these phenomena to it are examined. The conclusion is reached, on the basis of available evidence, that they are to be considered as indirect disorders of the body image. The direct disorders of the body scheme are reviewed and analyzed in this connection. The differentiation between the two groups of disorders and their particular characteristics is indicated. An attempt is made to categorize the various disturbances in the sphere of body scheme that have been observed with organic conditions.

In approaching the subject from a clinical-phenomenologic standpoint, the following classification of the diverse manifestations of body disorientation referable to the body scheme is arrived at: 1. Autotopopagnosia, or somatotopagnosia, i. e., general disorientation and lack of recognition in the sphere of the body and in the interrelation of its individual parts. 2. Finger agnosia, i. e., primary specific disorientation and loss of recognition in the sphere of the fingers of both hands and in their spatial relationship. 3. Agnosia for laterality in the somatic sphere, i. e., disorientation for right and left of the body (usually associated with either of the two conditions just mentioned). 4. Anosognosia, i. e., lack of knowledge of disease, most frequently observed with left cerebral hemiplegia. Disturbance in orientation for laterality, if present, refers to the diseased side only. 5. Autosomatamnesia and autosomatagnosia, respectively, i. e., amnestic and agnostic unawareness of the impaired parts or half of the body, varying in degree from simple neglect of their presence to the experience of their nonexistence. Disorientation for laterality, if demonstrable, is related to the nonappreciated side. 6. Somatoparaphrenia, i. e., specific psychic elaboration (marked by formation of illusions, confabulations and delusions) with respect to the affected members or side of the body, believed or experienced as absent. 7. Fantom limb, i. e., nonrealization of actual absence or experience of possession of a lost member of the body.

I believe that the study of the body scheme and its disorders associated with lesions of the brain should be given more attention than has hitherto been accorded it. The fundamental importance of the facts emerging from the study of these disorders for an understanding of many an obscure phenomenon in the fields of neurology and psychiatry is emphasized.

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STUDIES ON THE CORPUS CALLOSUM

VI. ORIENTATION (TEMPORAL-SPATIAL GNOSIS) FOLLOWING SECTION OF THE CORPUS CALLOSUM

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For many years numerous investigators have made efforts to establish a clinical syndrome for the recognition of lesions in the corpus callosum. Mingazzini,[1] from a study of personal cases and those reported in the literature, expressed the opinion that mental symptoms predominate with callosal lesions. Memory disturbances, especially for recent events, have been stressed by many investigators. Collier [2] expressed the belief that "mental reduction" was most constant with lesions involving the splenium. Niessl von Mayendorf [3] stated that disturbances of orientation may be due to interruption of the commissural fibers between the two occipital lobes, that is, to lesions of the posterior portion of the corpus callosum. Foix and Masson [4] observed disorientation in cases of thrombosis of the posterior cerebral arteries in which the splenium of the corpus callosum was destroyed. However, they could not form any conclusion as to the relative importance of the splenial lesion in the production of the disorientation, since involvement of the occipital lobes was present coincidentally. Meyer [5] studied a case of the Korsakoff psychosis in which lesions in the splenium and both occipital lobes were present. Cramer [6] found acute episodes of mental confusion in the 2 cases of splenial tumor and disturbances in recent memory in 3 of the 4 remaining cases of neoplasm of the corpus

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1. Mingazzini, G.: Der Balken, Berlin, Julius Springer, 1922.

2. Collier, J.: Localization of Function in the Nervous System, Brit. M. J. **1**:55, 1930.

3. Niessl von Mayendorf, E., cited by Oppenheim, H.: Lehrbuch der Nervenkrankheiten, ed. 6, Berlin, S. Karger, 1913, p. 947.

4. Foix, C., and Masson, A.: Le syndrome de l'artère cérébrale postérieure, Presse méd. **31**:361, 1923.

5. Meyer, A.: Personal communication to the author.

6. Cramer, F.: Clinical Diagnosis of the Tumors of the Corpus Callosum, Bull. Neurol. Inst. New York **5**:37, 1936.

callosum. He interpreted these disturbances as representing the failure of the corpus callosum to function in the making of new memory associations, or engrams. Mingazzini [1] cited several authors (Redlich; Steinert; Pfeiffer, and others) who have discussed in detail disturbances of orientation associated with callosal lesions. He concluded that there was insufficient evidence to prove that functional disturbances of the corpus callosum are likely to produce a Korsakoff syndrome.

The studies cited are concerned with tumors and vascular accidents which result inevitably in damage to adjacent structures. Marchiafava's disease (primary degeneration of the corpus callosum) is usually characterized by severe intellectual deterioration (King and Meehan [7]), but probably factors of arteriosclerosis and nutritional deficiency complicate the clinical picture. As far as I can find in the literature, the only case of a Korsakoff-like psychosis occurring after surgical section of the splenium was reported by Trescher and Ford.[8]

The present study is concerned with the study of temporal-spatial relationships in a group of epileptic patients in whom the corpus callosum was sectioned partially or completely. These patients presented the unique opportunity of studying all aspects of orientation before and after operation.

METHODS AND PROCEDURE

The surgical procedure has been described by Van Wagenen and Herren.[9] Dr. W. P. Van Wagenen performed the craniotomy in all cases, which, unless otherwise noted, was over the right frontoparietal region. All the patients were native Americans of the Caucasian race. Essentially the same tests were made before and at variable intervals after operation.

Spatial relationships were studied by various methods. The ability to localize objects absolutely and relatively in each homonymous visual field was studied in the manner described previously.[10] Depth perception was exhaustively studied by Dr. Karl U. Smith. Localization of an auditory stimulus was evaluated by testing the subject's ability, while blindfolded, to localize the sound of a play frog in the median plane. As regards body orientation, the following aspects were studied: right-left orientation; ability to name various parts of the patient's body touched by the examiner while the patient was blindfolded; ability to name, point out

7. King, L. S., and Meehan, M. C.: Primary Degeneration of the Corpus Callosum, (Marchiafava's Disease), Arch. Neurol. & Psychiat. **36**:547 (Sept.) 1936.

8. Trescher, J. H., and Ford, F. R.: Colloid Cyst of the Third Ventricle: Report of a Case; Operative Removal with Section of the Posterior Half of Corpus Callosum, Arch. Neurol. & Psychiat. **37**:959 (April) 1937.

9. Van Wagenen, W. P., and Herren, R. Y.: Surgical Division of Commissural Pathways in the Corpus Callosum: Relation to Spread of an Epileptic Attack, Arch. Neurol. & Psychiat. **44**:740 (Oct.) 1940.

10. Akelaitis, A. J.: Studies on the Corpus Callosum: II. The Higher Visual Functions in Each Homonymous Field Following Complete Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **45**:788 (May) 1941.

and move parts of the patient's own body or that of others on request, and in the proprioceptive functions (appreciation of position and passive movement of the extremities) as tested in the regular neurologic examination. Spatial orientation was studied in such psychobiologic acts as the ability of the patient to find his way about in the hospital or about the city and in the analysis of the routes to be taken to get from one town to another by means of an automobile map. Since many of these patients lived in towns outside Rochester, they were questioned as to the route used to reach the hospital from their homes. The patient was required to draw a plan of the examiner's office (in which he was present at the time) and also one of his room in the hospital or at home from memory. Constructional praxis (Kleist) was studied by the patient's ability to draw geometric (bidimensional and tridimensional) figures. A much more detailed study by the Kohs block test was made by Parsons.[11]

Time gnosia was studied in various ways. The patient's judgment of the passage of time, such as the time of day or the day of the week or month, was noted. His memory for recent and remote events and his retention for immediate events as studied by digit recall, paired words and recall of phrases were all studied in the manner used in the average psychiatric examination (Muncie[12]). His sense of rhythm was studied by such means as tapping out a march, ability to carry a tune, appreciation of music, and, when occasion allowed, dancing and instrument playing.

To study time gnosis unilaterally a toy clock was used. The test is performed with the subject blindfolded. He is given the orientation that 6 is toward him and 12 is toward the examiner, who sits opposite. He is requested to tell the time as he interprets it by feeling the hands of the clock, which have been set by the examiner. The right hand is first tested and then the left. The patient is then required to set the clock hands with each hand separately to the time requested by the examiner. This test, of course, utilizes the study of fine complex movements, appreciation of differences in size of the clock hands, left-right orientation and spatial relationships.

The ability to synthesize the comprehended elements of several processes into a whole was studied. Disturbance in this ability was designated as simultagnosia by Wolpert.[13] The recognition of card combinations when playing such games as poker and pinochle was evaluated. Various cards depicting an integrated story, such as a bee and a flower or an automobile and a policeman on a motorcycle, were presented to the subject for interpretation. The pictorial completion test II of Healy[14] was utilized. Ability to give the content or plot of brief stories read by the patient and to the patient was evaluated. The subject's ability to comprehend and enjoy cinematography, the theater and radio plays was studied whenever occasion allowed.

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11. Parsons, F. H.: Psychological Tests of Patients One Year After Section of the Corpus Callosum, Psychol. Bull. **37**:498, 1940.

12. Muncie, W.: Psychobiology and Psychiatry: A Textbook of Normal and Abnormal Human Behavior, St. Louis, C. V. Mosby Company, 1939.

13. Wolpert, I.: Die Simultagnosie (Störungen der Gesamtauffassung), Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:397, 1924.

14. Healy, W.: Pictorial Completion Test II., J. Applied Psychol. **5**:225, 1921; in Bronner, A. F.; Healy, W.; Lowe, G. M., and Shimberg, M. E.: A Manual of Individual Mental Tests and Testing, Boston, Little, Brown & Company, 1938.

Elaborate laterality studies were made. Handedness is designated as H, footedness as F and eyedness as E. In cases in which a tendency toward ambilaterality existed, the first letter implies that this hand was used predominantly in highly skilled activities, such as writing. Thus L/RH means that, although able to perform many tasks with the right hand, the patient wrote with his left hand.

REPORT OF CASES[15]

The cases were classified as follows:

Group I.—Complete section of the corpus callosum (cases 1 to 8).

A. Normal neurologic signs (cases 1 and 2).

B. Evidence of unilateral cerebral damage before operation (cases 3 to 7).

1. Anterior portions of cerebrum predominantly involved (cases 3 to 5).
2. Posterior portions of cerebrum predominantly involved (cases 6 and 7).

C. Evidence of diffuse involvement of the brain (case 8).

Group II.—Section (partial or complete) of the corpus callosum in cases with postoperative evidence of cerebral damage (cases 9 to 11).

A. Partial section of the corpus callosum (cases 9 and 10).

B. Partial and subsequently complete section of the corpus callosum (case 11).

Group III.—Partial section of the corpus callosum (cases 12 to 26).

A. Normal neurologic signs (cases 12 to 21).

B. Evidence of unilateral cerebral damage before operation (cases 22 to 25).

1. Anterior portions of cerebrum predominantly involved (cases 22 to 24).
2. Posterior portions of cerebrum predominantly involved (case 25).

C. Evidence of diffuse involvement of the brain (case 26).

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15. These cases have been reported in greater detail with regard to different aspects of psychobiologic activity in other articles. (*a*) Akelaitis, A. J.; Risteen, W. A.; Herren, R. Y., and Van Wagenen, W. P.: Studies on the Corpus Callosum: III. A Contribution to the Study of Dyspraxia and Apraxia Following Partial and Complete Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **47**:971 (June) 1942. (*b*) Van Wagenen, W. P., and Herren, R. Y.: Surgical Section of Commissural Pathways in the Corpus Callosum: Relation to Spread of an Epileptic Attack, ibid. **44**:740 (Oct.) 1940.

GROUP I: COMPLETE SECTION OF THE CORPUS CALLOSUM

A. NORMAL NEUROLOGIC SIGNS (fig. 1)

CASE 1 (case 8[15a]).—E. J. B., a deteriorated, unmarried white woman aged 24, was admitted to the Rochester Municipal Hospital March 11, 1939. She had had grand mal seizures for fourteen years and violent psychomotor attacks for six years, associated with marked personality changes. She was dull and apathetic and showed memory impairment. The Binet level was 11 years. The neurologic status was normal. Laterality studies revealed right ocular dominance, right handedness and right footedness.

First Operation.—On March 18 the body and the posterior half of the genu of the corpus callosum were sectioned.

Course.—The patient showed no changes in her behavior, and the Binet level was 10 years 4 months on April 3. She continued to have seizures.

Second Operation.—On April 24 the remainder of the corpus callosum was divided.

Course.—No changes in the mental or neurologic status could be observed. The Binet level remained at 10 years 4 months. Convulsions and psychomotor attacks continued, and she was admitted to the Rochester State Hospital for the second time. She has shown no greater difficulty with memory and orientation than before operation. In her psychomotor attacks she is, of course, severely confused and hallucinated. The Binet level in June 1940 was 10 years 7 months.

CASE 2 (case 18[15a]).—G. E., a white married farmer aged 35, was admitted to the Strong Memorial Hospital May 2, 1940. He had had poliomyelitis, with residual weakness of the right leg, in childhood, and in 1933 osteomyelitis of the right tibia and lower portion of the femur developed, which necessitated a midthigh amputation in 1938. On August 1937 convulsions and right-sided paralysis appeared, with an emissive form of aphasia. Dr. W. P. Van Wagenen drained an abscess in the left frontal lobe of the brain, and the aphasia and hemiplegia cleared. Neurologic examination revealed slight exaggeration of tendon reflexes in the right upper extremity and a speech disorder consisting of a stutter and a mild emissive type of aphasia.

Laterality studies revealed right handedness and right ocular dominance.

Operation.—On May 17 the corpus callosum was completely sectioned.

Course.—The postoperative course was uneventful. No evidence of disorientation was ever noted. The stutter and dysphasia remained unchanged.

B. EVIDENCE OF UNILATERAL CEREBRAL DAMAGE BEFORE OPERATION (fig. 1)

1. *Anterior Portions of Cerebrum Predominantly Involved.*—CASE 3 (case 10[15b]).—G. B., a white boy aged 14, was admitted to the Rochester Municipal Hospital May 8, 1939. After an attack of diphtheria at the age of 2 years left hemiplegia developed and persisted. Grand mal and petit mal seizures had been present since the age of 3. He was mentally retarded, the Binet level being 9 years 3 months (intelligence quotient 64). Neurologic examination revealed pronounced spastic hemiplegia of the left side, with athetosis and chronic dorsal flexion of the left big toe. Laterality studies revealed right handedness, right footedness and right ocular dominance.

First Operation.—On May 19 the corpus callosum was sectioned completely. The left limb of the fornix was cut just above the foramen of Monro. In the

inferior portions of areas 4 and 6 of the right frontal lobe and over the superior temporal convolution, directly below, a large area of thickened pia-arachnoid was observed.

Course.—The patient continued to have seizures. The Binet level two weeks after operation was 10 years 1 month (intelligence quotient 69). There was no evidence of disorientation in the spatial or temporal sphere. The neurologic status remained unchanged. He was readmitted Nov. 11, 1939 for excision of the right frontal lobe. His status at this time was essentially the same as on his first admission except for a rather remarkable increase in size and moderate depression of mood.

Second Operation.—On November 30 the right frontal lobe was resected.

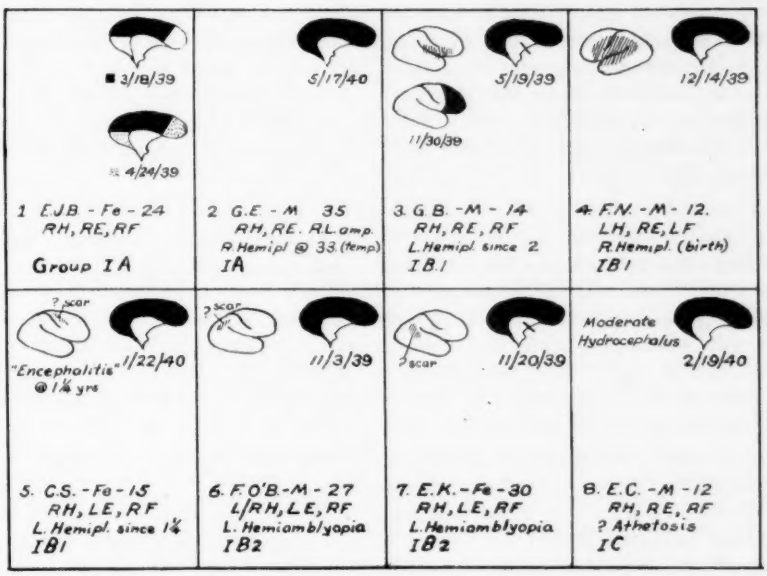

Fig. 1 (group 1).—Patients with complete section of the corpus callosum. *A*, patients with normal neurologic signs; *B*, patients with evidence of unilateral cerebral damage before operation, involving predominantly, the anterior (*1*) or the posterior (*2*) portion of the cerebrum, and *C*, patients with evidence of diffuse involvement of the brain.

Subsequent Course.—Seizures have continued but are much less severe and are rather infrequent. The patient is well oriented in all spheres, enjoys the cinema and radio plays and spends much time at home listening to musical programs over the radio.

Case 4.—F. N., a white boy aged 12, was admitted to the Rochester Municipal Hospital Nov. 26, 1939. After a prolonged labor, in which the mother had numerous eclamptic convulsions, the patient had been delivered spontaneously. For the first three days of life he had convulsions and high fever, which left him with right cerebral palsy. Since the age of 2 he had had grand mal and petit mal seizures, with increasing frequency. For the past two years he had become a

serious behavior problem, his activity being characterized chiefly by cruelty to younger children. He was committed to a colony for epileptic patients in August 1939. He was mentally retarded, the Binet level being 10 years 2 months (intelligence quotient 86). Neurologic studies revealed typical right hemiplegia, with slight athetosis and hypesthesia to all forms of sensation, and hight homonymous hemianopia. Laterality studies revealed left handedness, left footedness and right ocular dominance.

Operation.—On December 14 a left midparietal craniotomy was performed, and the corpus callosum was completely sectioned. The body of the corpus callosum was extremely thin. The left cerebral hemisphere was very thin, being not over 4 mm. in thickness. This atrophy was over the region of distribution of the left middle cerebral artery.

Course.—The patient showed no evidence of disorientation at any time. The Binet level on Jan. 19, 1940 was 10 years 5 months (intelligence quotient 85). The patient continued to have attacks of jacksonian epilepsy involving the right side, without loss of consciousness, but had no grand mal seizures. His behavior remained incorrigible, and he was committed to the Rochester State Hospital on June 13, 1940. While there he has shown no evidence of disorientation. In August 1941 the Binet level was 11 years 4 months (intelligence quotient 85).

CASE 5 (case 16 [15n]).—C. S., a white girl aged 15, was admitted to the Strong Memorial Hospital Jan. 4, 1940. At 15 months of age she had "encephalitis," which left her left side paralyzed. Petit mal attacks began at the age of 5 years, and at 11 years grand mal seizures developed. She showed residual left hemiplegia, with some atrophy, slight spasticity and very infrequent athetoid movements on the left side. Sensation, including stereognosis and tactile lexia, was intact. She was cheerful, rather affectionate and mentally retarded, with a Binet level of 12 years 4 months (intelligence quotient 81). Laterality studies revealed right handedness, right footedness and left ocular dominance.

Operation.—On January 22 the corpus callosum was completely sectioned. The cortex showed a moderate degree of atrophy.

Course.—A transitory grasp reflex and ideokinetic dyspraxia developed in the left hand and lasted about three weeks. Definite hypesthesia prevailed over the left side, and she showed astereognosis and tactile alexia in the left hand.

Twenty-four hours after operation she denied having been operated on and could not recall the name of the hospital, but orientation for persons and remote memory was good. She was uncomfortable, complaining of numbness and weakness of her left side. One week after operation she was feeling better and showed no disorientation. One month later detailed studies of orientation revealed that the only disturbance in orientation present since operation was inability to read or set the clock hands with the left hand. She has been examined on numerous occasions since (the last being in April 1941), and this defect persists. Coincidentally, sensory tests revealed that two point discrimination, tactile lexia and stereognosis were disturbed in the left hand. A psychometric test performed in March 1940 (two months after operation) revealed a Binet level of 11 years 11 months (intelligence quotient 79).

2. *Posterior Portions of Cerberum Predominantly Involved.*—CASE 6 (case 9 [15a]).—F. O'B., a white married man aged 27, was admitted to the Strong Memorial Hospital Oct. 11, 1939. At the age of 13, one year after a trauma to the head, grand mal seizures developed, which had continued. In recent years he had become a periodic drinker. Neurologic examination revealed left hemiamblyopia.

Laterality studies revealed ambidexterity, with dominance of the left hand, right footedness and left ocular dominance. Ventriculograms revealed dilatation of the right ventricle, and electroencephalograms disclosed bursts of delta waves over the right temporoparieto-occipital region.

Operation.—On November 3 the corpus callosum was completely sectioned.

Course.—During the first week he was hostile and mildly confused, especially at night. Later he commented on almost complete amnesia for events during the first ten days after operation. Subsequently, he has shown no evidence of disorientation except for a disturbance in absolute orientation in the hemiamblyopic field, which was present before operation.

CASE 7 (case 10 [15a]).—E. K., a white single woman aged 30, was admitted to the Rochester Municipal Hospital Nov. 6, 1939. At the age of 17, two years after an injury to the head, grand mal seizures developed. These usually occurred shortly after falling asleep and began with a numb feeling in the left arm. Neurologic examination revealed left homonymous hemiamblyopia and questionable atrophy of the left arm. Laterality studies revealed right handedness, right footedness and left ocular dominance. Ventriculograms revealed marked dilatation of the temporal and occipital horns and the posterior end of the body of the right ventricle. Electroencephalograms disclosed that delta waves were of greatest amplitude over the right temporoparieto-occipital region.

Operation.—On November 20 the corpus callosum was completely sectioned.

Course.—For the first two weeks after operation the patient was in a pseudo-cataleptoid state, being mute and apparently confused. Her mental condition gradually cleared, and she admitted that she had little recollection of events during those two weeks. She remarked that she began to recognize members of her family on December 1. On December 4 she drew correctly a plan of her room. On December 13 detailed studies of orientation revealed essentially the same condition as before operation. She performed the clock test correctly with either hand.

The nature of the seizures has changed. At present they are of jacksonian type and are limited to numbness over her left side, followed by clonic and tonic movements in this side, but with no loss of consciousness. She has been examined on numerous occasions since her discharge, the last examination being in August 1941. No evidence of disorientation has been observed.

C. EVIDENCE OF DIFFUSE INVOLVEMENT OF THE BRAIN (fig. 1)

CASE 8 (case 17 [15a]).—E. C., a white boy aged 12, was admitted to the Strong Memorial Hospital Feb. 15, 1940. He had had trauma to the head, without loss of consciousness, at 2 and 5 years of age. At 7 he began to have petit mal seizures, and at 10 grand mal seizures developed. Physical status revealed enlarged tonsils and a few carious teeth. The neurologic status fluctuated; he appeared cataleptoid at times; infrequently athetoid-like movements were seen, and occasionally increased tendon reflexes, with a positive Babinski sign, were found on the left side. Vision in the left eye was 6/60. He was an irritable, attention-gaining boy, with a talent for drawing. His Binet level was 10 years 10 months (intelligence quotient 86). Laterality studies revealed right handedness, right footedness and right ocular dominance. A ventriculogram showed uniform dilatation of the entire ventricular system.

Operation.—On February 19 the corpus callosum was sectioned completely. Judging from the enlarged subarachnoid spaces, the cortex appeared to be slightly atrophied.

Course.—The postoperative period was complicated by frequent attacks with loss of consciousness, which may be designated as "terror spells." These attacks produced fluctuating neurologic and psychobiologic signs, making it impossible to evaluate the clinical picture resulting purely from section of the corpus callosum. For a variable period after one of these seizures he would be confused.

Toward the end of his stay in the hospital he showed slight right hemiparesis with hyperesthesia and dysesthesias in the right arm. At this time he was well oriented, found his way about the hospital and remembered easily the names of the nursing staff in a division in which he had been before his operation. However, he showed deterioration in mental ability, and the Binet level, two months after operation, was 9 years 3 months (intelligence quotient 71). His drawings had deteriorated considerably; how much this was due to the right hemiparesis is difficult to ascertain. He showed no difficulty in perspective, however, and figures in two and three dimensions were correctly drawn.

After discharge, on April 17, 1940, he continued to have "terror spells," especially at night, but less frequently. He became docile, a striking change from his preoperative behavior. In January 1941 he fell down a flight of stairs during a grand mal seizure, and since then he has stuttered. In March 1941 he was studied in detail. Neurologic examination revealed bilaterally equal deep reflexes, equal strength of the hand grips, an infrequent Babinski response on the left side and marked adiadokokinesis in the right hand. In the right hand there were impairment of the ability to name the fingers touched while he was blindfolded and disturbance of two point discrimination. For the first time since operation he was able to perform the clock test correctly with either hand. His drawing had improved a good deal and was as satisfactory as before operation. He was well oriented, enjoyed the cinema and the serials on the radio and was able to draw accurately a plan of the office and his cubicle with proper relations to other parts of the hospital. The Binet level was 10 years (intelligence quotient 72).

GROUP II: SECTION (PARTIAL OR COMPLETE) OF THE CORPUS CALLOSUM IN PATIENTS WHO SHOWED POSTOPERATIVE EVIDENCE OF CEREBRAL DAMAGE

A. PARTIAL SECTION OF THE CORPUS CALLOSUM (fig. 2)

CASE 9 (case 11 [15a]).—W. S., a white farmhand aged 27, was admitted to the Strong Memorial Hospital on Feb. 14, 1939. After an injury to the head he had had grand mal seizures for the past ten years. The neurologic status was normal. Laterality studies revealed right handedness, right footedness and right ocular dominance.

First Operation.—On February 22 a right midparietal craniotomy was performed and the body of the corpus callosum sectioned.

Course.—Left hemiparesis with left-sided and generalized seizures developed.

Second Operation.—On February 27 the wound was reopened and the posterior half of the genu divided. Retrograde thromboses in the ligated veins were observed.

Course.—The hemiparesis, with slight weakness of the lower part of the face, continued on the left side. He showed psychomotor retardation but continued to be efficient in his card playing, and there was no evidence of confusion with formal tests. He was, however, unable to play his steel guitar and had apparently lost all sense of rhythm in music. The seizures continued.

Third Operation.—On May 4 the old wound was reopened, and the remainder of the corpus callosum except for the last centimeter of the splenium was sectioned. The right fornix was divided.

Course.—No disorientation was observed subsequently. The disturbance in music continued unchanged.

CASE 10 (case 12 [15a]).—L. C., a 17 year old Italian lad, was admitted to the Strong Memorial Hospital July 1, 1940. Four months after a compound fracture of the skull, in 1936, there developed grand mal seizures, associated with an aura of flashes of light in the right homonymous field and right-sided jacksonian attacks. The patient was obese and had borderline intelligence. Examination of the visual fields showed right homonymous hemianopia. In July 1939 the left occipital lobe was resected by Dr. Van Wagenen, after which right hemiparesis developed. This cleared up after evacuation of a subdural clot. The convulsions continued. Laterality studies revealed right handedness, right footedness and transfer of ocular dominance from right to left after lobectomy.

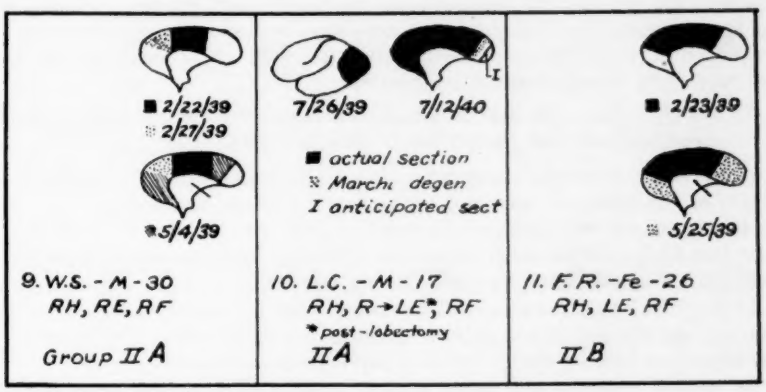

Fig. 2 (group II).—Patients with partial or complete section of the corpus callosum and postoperative evidence of cerebral damage. *A*, partial section of the corpus callosum; *B*, partial or subsequent complete section of the corpus callosum.

Operation.—On July 12 the entire corpus callosum with the exception of the tip of the splenium was sectioned.

Course.—Right-sided seizures and left hemiparesis developed. Although no detailed orientation studies were made, no obvious confusion was observed. Ten days after operation the patient died during a severe right-sided seizure.

Autopsy disclosed a large subdural hematoma over the right frontal lobe.

B. PARTIAL AND SUBSEQUENTLY COMPLETE SECTION OF THE CORPUS CALLOSUM (fig. 2)

CASE 11 (case 13 [15a]).—F. R., a single white woman aged 26, was admitted to the Strong Memorial Hospital Feb. 19, 1939. She had Erb's birth palsy on the left side and had been treated for congenital syphilis, with good results. Grand mal seizures had been present since the age of 2. She played the piano rather well. The physical status disclosed widely separated, peglike teeth and an infantile uterus

Neurologic examination revealed horizontal nystagmus on lateral deviation of the eyes, absence of the left biceps reflex and atrophy of the left arm with contraction of the biceps muscle. The serologic reactions of the blood and spinal fluid were normal. Laterality studies revealed right handedness, right footedness and left ocular dominance.

First Operation.—On February 23 a midparietal craniotomy was performed on the right side, and the body and the posterior half of the genu of the corpus callosum were sectioned.

Course.—Left hemiparesis with sensory changes developed. The patient was depressed and apprehensive. For the first two weeks after operation she showed mild disturbances in sensorium and spoke of herself in the third person. When asked how she felt she would reply: "F. has a headache today" or "F. doesn't feel well today." One month after operation she became panicky, with ideas of reference and preoccupation. Gross tests showed no evidence of disorientation.

After discharge to her home on March 26, a temporary state of diagnostic dyspraxia developed. Her concentration and memory for recent events were impaired; she was greatly depressed and expressed many feelings of inadequacy and hopelessness. Grand mal seizures continued, and she was readmitted to the hospital on May 23. Neurologic examination revealed left hemiparesis. She was not confused in temporal-spatial relationships.

Second Operation.—On May 25 the old wound was reopened, and the remainder of the corpus callosum and the left fornix were sectioned.

Course.—The depression continued unabated. No evidence of disorientation could be elicited. Hemiparesis improved to the extent that she was able to write with the left hand, and stereognosis was intact on this side. After discharge to her home June 11, in addition to her depression, irritability, seclusiveness and mysophobia developed. She was unable to crochet or play the piano.

In September 1939 she was studied in detail. No disturbance of orientation was observed, and she was able to perform the clock test satisfactorily with either hand. The depression lessened after a series of psychotherapeutic sessions.

In August 1940 she was again studied. The depression was gone, and she was able to play the piano well. There was no difficulty with memory or orientation.

GROUP III: PARTIAL SECTION OF THE CORPUS CALLOSUM

A. NORMAL NEUROLOGIC SIGNS (fig. 3)

CASE 12 (case 2 [15a]).—E. L., a single white man aged 22, was admitted to the Rochester Municipal Hospital Nov. 29, 1939. Petit mal attacks began at 5 and grand mal attacks at 15 years of age. He was a vague, circumstantial talker, with a Binet level of 14 years 10 months (intelligence quotient 92). The physical and neurologic status was normal. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On Jan. 5, 1940 the body of the corpus callosum was sectioned.

Course.—For the first week the sensorium appeared clouded, probably due to petit mal seizures. He then began to have grand mal attacks, usually related to visits of the mother, a highly irritating person. Three weeks after operation, detailed studies of orientation revealed no defects. He has been studied on numerous occasions since, and, except in periods just before or after a seizure, he is well oriented. On February 9 the Binet level was 13 years 11 months (intelligence quotient 87). In January 1941 the Binet level was the same as before.

CASE 13.—L. M., a 14 year old white boy, was admitted to the Strong Memorial Hospital May 16, 1941. At the age of 7 he was struck over the left temporal area with a baseball bat. This was followed by attacks of twitchings of the face. Two years prior to admission he began to have grand mal attacks. The neurologic status was normal. The Binet level was 14 years 7 months. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On June 12 the corpus callosum was sectioned from the rostrum to the point where the fornix joins the body of the corpus callosum. The right and left fornices were also divided.

Course.—Postoperative recovery was uneventful, and no evidence of disorientation was observed. On July 3 the Binet level was the same as before operation.

CASE 14.—J. W., a deteriorated, obese white girl aged 17, was admitted to the Strong Memorial Hospital July 4, 1941. At the age of 2 left-sided seizures developed, which later became generalized. The neurologic status was normal.

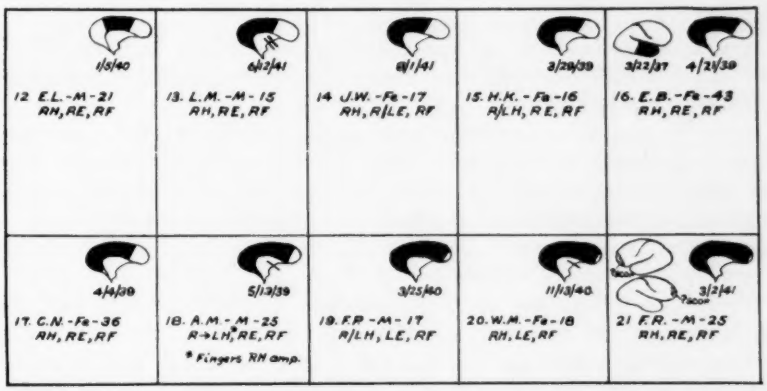

Fig. 3 (group III-A).—Patients with normal neurologic signs and with partial section of the corpus callosum.

The Binet level was 9 years 2 months (intelligence quotient 57). Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On August 1 the corpus callosum was sectioned from the rostrum to the point at which the fornix meets the body of the corpus callosum anteriorly.

Course.—She showed no psychobiologic change. She continued to have temper tantrums associated with resistiveness, combativeness and profanity. She was surprisingly skilful in sewing and cutting out cloth from patterns to make dresses and men's shirts. The Binet level on August 26 was 8 years 9 months (intelligence quotient 55).

CASE 15 (case 1 [15a]).—H. K., a pleasant, intelligent white girl aged 16, was admitted to the Strong Memorial Hospital March 12, 1939. Convulsions began at the age of 3, but in the past two years they had become increasingly frequent. She was adept at playing the piano and the French horn. The physical and neurologic status was normal. Laterality studies revealed mixed handedness, right footedness and right ocular dominance.

First Operation.—On March 29 the genu and body of the corpus callosum were sectioned.

Course.—Convalescence was slow, and no disturbance in orientation was elicited. She was able to play the piano and the French horn as efficiently as before operation. Because of a return of the seizures she was readmitted to the hospital on June 23, 1939.

Second Operation.—On July 5, as the original bone flap was being turned down, the patient died. Permission for autopsy could not be obtained.

CASE 16 (case 4 [15a]).—E. B., a single white woman aged 43, a former secretary, was admitted to the Strong Memorial Hospital April 17, 1939. For the past six years she had had grand mal, petit mal and "hysterical" attacks. In 1937 Dr. Van Wagenen resected the anterior two thirds of the right temporal lobe, which contained a fibrillary astrocytoma. The physical and neurologic status was normal. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On April 21 the genu and body of the corpus callosum were sectioned.

Course.—Convalescence was rapid. The patient remained well oriented. She has been followed intensively since discharge from the hospital and has shown no evidence of disorientation.

CASE 17 (case 3 [15a]).—C. N., a white single woman aged 36, a former school teacher, was admitted to the Strong Memorial Hospital March 23, 1939. Grand mal, petit mal and psychomotor attacks had been present for the past ten years. Physical examination revealed a saccular type of bronchiectasis in the left lung. The neurologic status was normal. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On April 4 the corpus callosum was sectioned from just above the anterior commissure to a point within 2 cm. of the tip of the splenium.

Course.—The patient was confused for the first two days. After a series of jacksonian seizures involving both sides, transitory weakness of the left hand and urinary incontinence developed. The latter, together with heavy sedation, contributed to making her depressed. She showed no disorientation subsequently. In July 1940, during observation in a violent psychomotor attack, she was extremely confused.

CASE 18 (case 5 [15a]).—A. M., a white single man, a former gardener and mill hand was admitted to the Strong Memorial Hospital May 7, 1939. He had been subject to grand mal seizures for the past ten years. One year ago the fingers of the right hand were amputated accidentally. The neurologic status was normal except for irregular pupils, which reacted poorly to light. Serologic studies of the blood and spinal fluid gave negative results. Laterality studies revealed a shift from right to left handedness, right footedness and right ocular dominance.

Operation.—On May 13 the corpus callosum was sectioned completely except for the posterior centimeter of the splenium. The left fornix was divided.

Course.—For the first two weeks after operation the patient had fever (with a temperature of 40 C. [104 F.]), of undetermined origin. During this period he was confused, especially at night. Subsequently no evidence of disorientation was observed.

CASE 19 (case 6 [15a]).—F. P., an Italian boy aged 17, was admitted to the Rochester Municipal Hospital March 19, 1940. Petit mal attacks coincident with

development of obesity began ten years ago. In the past five years grand mal seizures and behavior changes had occurred. He was mentally retarded, with a Binet level of 11 years 10 months (intelligence quotient 74). Physical examination revealed a pituitary type of obesity. The neurologic status was normal. The sella turcica was small. Laterality studies revealed mixed handedness, right footedness and left ocular dominance.

Operation.—On March 22 a frontoparietal craniotomy was performed on the left side, and the entire corpus callosum except for the tip of the splenium was sectioned.

Course.—The patient showed no evidence of disorientation. He tap-danced and played the piano as efficiently as before operation. The Binet level was 13 years (intelligence quotient 80) on April 11.

CASE 20 (case 7 [15a]).—W. M., a white, single girl aged 18, was admitted to the Strong Memorial Hospital Nov. 2, 1940. At the age of 13 months she sustained a fracture of the right parietal region, followed by temporary left hemiplegia. One year later grand mal seizures began. These were usually preceded by numbness and weakness of the left side. She was pleasant and mentally retarded. The Binet level was 11 years 1 month (intelligence quotient 70). The physical status was normal. The neurologic status was usually normal, although occasionally hypesthesia from the angle of the jaw down and slightly exaggerated tendon reflexes were observed on the left side. Laterality studies revealed right handedness, right footedness and left ocular dominance.

Operation.—On November 13 the corpus callosum was completely sectioned except for a few possible fibers in the splenium. The left fornix was divided.

Course.—Except for slight weakness and astereognosis in the left hand for the first two days after operation, her convalescence was uneventful. Although of borderline intelligence, she was adept at the tests for orientation, including the clock test. The Binet level was 10 years 9 months (intelligence quotient 67) on December 3.

CASE 21.—F. R., a single white man aged 26, was admitted to the Strong Memorial Hospital Feb. 9, 1941. In May 1939 he was struck by an automobile and sustained a severe compound fracture of the frontal portions of the skull, with bilateral destruction of the frontal lobe. In November 1940 he began to have grand mal seizures. Physical examination revealed facial defects as a result of his injury. Neurologic examination disclosed color blindness for red and green and weakness of the external ocular muscles on the left side. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On March 2 the corpus callosum was sectioned completely except for a few possible fibers in the tip of the splenium.

Course.—This was uneventful except for some muteness for the first week, caused by a severe headache, which was accentuated on talking. Disorientation was never observed. He has had no further seizures and is now occasionally employed as a laborer.

B. EVIDENCE OF UNILATERAL CEREBRAL DAMAGE BEFORE OPERATION (fig. 4)

1. *Anterior Portions of Cerebrum Predominantly Involved.*—CASE 22 (case 4 [15b]).—R. M., a white boy aged 10 years, was admitted to the Rochester Municipal Hospital Feb. 27, 1939. He had had grand mal seizures for the past nine years and status epilepticus on several occasions. Because of combativeness, he had been placed

in a colony for epileptic patients for the past two years. Neurologic status revealed Erb's birth palsy on the right side and left hemiplegia, with weakness of the left internal rectus muscle. He was mentally retarded, with a Binet level of 7 years 6 months (intelligence quotient 71). Laterality tests revealed right handedness and right footedness. Ocular dominance was not tested.

Operation.—On March 4 the body of the corpus callosum was sectioned.

Course.—Postoperative convalescence was uneventful. A psychometric test, three weeks after operation, revealed a Binet level of 7 years 4 months (intelligence quotient 70). He became more docile and returned to school, where his teachers went into ecstasies over his satisfactory progress. He showed no obvious disturbance of orientation at any time. He died in status epilepticus on Feb. 24, 1940.

Case 23 (case 1 [15 b]).—G. M. R., a white bachleor aged 34, was admitted to the Strong Memorial Hospital Feb. 6, 1939. He had cerebral birth palsy of the right side and had had grand mal seizures for the past ten years. He finished two years of college and was in charge of a welfare project in a small Kentucky town. The physical status was good. Neurologic examination revealed right homonymous hemianopia and severe right hemiplegia with sensory disturbances. Laterality

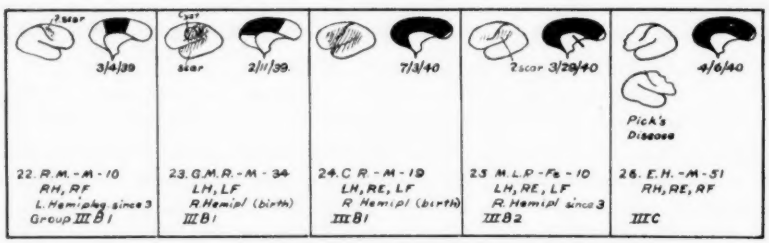

Fig. 4 (group III).—Patients with partial section of the corpus callosum and (*B*) with evidence of unilateral cerebral damage before operation, involving predominantly (*1*) the anterior or (*2*) the posterior portion of the cerebrum, or (*C*) with evidence of diffuse involvement of the brain.

tested revealed left handedness and left footedness. Ocular dominance was not tested.

Operation.—On February 11 a left parietal craniotomy was performed, and the body and posterior half of the genu of the corpus callosum were sectioned. A large porencephalic cyst in the posterior portion of the frontal lobe and excessive scar tissue over the two upper temporal convolutions and the parietal lobe were observed.

Course.—The patient convalesced satisfactorily and showed no evidence of disorientation. He has returned to welfare work and is self supporting.

Case 24.—C. R., a white youth aged 19, was admitted to the Strong Memorial Hospital June 20, 1940. He had had right cerebral palsy since birth, and in the past three months grand mal and petit mal seizures had developed. Neurologic examination revealed right hemiplegia, with the greatest involvement in the distal portion of the upper extremity. The Binet level was 12 years 10 months (intelligence quotient 80). Laterality studies revealed left handedness, left footedness and right ocular dominance.

Operation.—On July 3 the corpus callosum was entirely sectioned with the exception of a few fibers in the splenium.

Course.—Convalescence was uneventful. He showed no confusion. On August 10 the Binet level was 11 years 5 months (intelligence quotient 72) and in November it was 13 years (intelligence quotient 81).

2. *Posterior Portions of Cerebrum Predominantly Involved.*—CASE 25 (case 14 [15a]).—M. L. P., a white girl aged 10, was admitted to the Strong Memorial Hospital March 12, 1940. At the age of 3 years, after an injury to the head she went into status epilepticus and right hemiplegia with aphasia developed. The aphasia cleared in two months, and the paralysis improved. Six months before admission she began to have frequent petit mal attacks. The Binet level was 9 years 9 months (intelligence quotient 92). Neurologic examination revealed right homonymous hemiamblyopia, left external strabismus and residual right hemiplegia, with slight spasticity, exaggerated deep reflexes and a positive Babinski sign. Laterality studies revealed left handedness, left footedness and right ocular dominance. Encephalograms disclosed hydrocephalus of the left ventricle, especially its posterior portion. Electroencephalograms revealed a focus of abnormal discharge over the left parietal region.

Operation.—On March 29 the entire corpus callosum except the posterior 0.5 cm. of the splenium was sectioned. The left fornix was divided.

Course.—The early postoperative course was marked by perseveration in tasks and conversation, together with impairment of memory for recent events. On April 19 psychologic tests revealed a Binet level of 7 years 6 months (intelligence quotient 70). At home she showed memory defects and apathy. In November the Binet level was 8 years 8 months (intelligence quotient 78). She was unable to read or set the clock with her right hand, a difficulty which she did not show before operation. This was associated with inability to recognize forms or objects in her right hand, even though sensory tests were normal on this side. Insofar as other aspects of orientation were concerned, she was as well oriented as before operation.

C. EVIDENCE OF DIFFUSE INVOLVEMENT OF THE BRAIN (fig. 4)

CASE 26 (case 15 [15a]).—E. H., a white, married stock clerk aged 51, was admitted to the Strong Memorial Hospital March 26, 1940. For the past four years he has been subject to grand mal seizures, which occurred in series of several attacks. One week before admission he began to have seizures, and on admission was having an attack every fifteen minutes. In the attack adversive movements to the left, with the eyes in left conjugate deviation, generalized muscular twitchings and a prolonged howl occurred. In the intervals between attacks he was paraphasic and confused. Although the attacks ceased the next day, paraphasia continued until March 30. On April 2 he was confused and "catastrophe" reactions developed whenever difficult tests were made. He was able to copy complicated bidimensional figures but could not draw a cube, even though given numerous leads. Laterality studies revealed right handedness, right footedness and right ocular dominance.

Operation.—On April 6 the corpus callosum was completely sectioned except for a few possible fibers in the tip of the splenium. Advanced cortical atrophy, especially toward the frontal pole, was observed. Biopsy revealed diffuse loss of nerve cells throughout the third, fifth and sixth layers. With Cajal's silver stain, numerous round, argentophilic bodies were observed in the nerve cells and lying free in the parenchyma. These changes were suggestive of Pick's disease.

Course.—For two days the patient was semicomatose. For almost three weeks he had weakness of the left side, together with dyspraxia in the left hand. Throughout this period he was perplexed and apprehensive, and this state apparently became accentuated when the left side was studied. On April 27 he was tested in the examiner's office, but became extremely confused, with perseveration and urgency of urination and defecation. On April 30 he began to have numerous jacksonian fits involving the right side, and these continued for three days, after which right hemiplegia with aphasia appeared. Speech returned, and the hemiplegia cleared within a week. He left the hospital on May 9.

When seen on May 30 at his home by Dr. W. A. Risteen, the patient was greatly improved. He spontaneously commented on his lacunar amnesia during his stay in the hospital, but remembered the names of the staff well. He was correctly oriented.

In August 1940 he was studied in detail. He showed disturbances in calculation and defects in recent memory and immediate retention. However, his performance was better than when he was examined before operation, on April 2. He could draw three-dimensional figures and was correctly oriented. The clock test was well performed with each hand. The lacunar amnesia for certain intervals of his stay in the hospital persisted. The neurologic status was normal.

Comment on Cases.—For only 2 patients in this series with complete section of the corpus callosum were the neurologic signs normal, or at most significant of minimal disturbance, before operation. Patient 1 was a deteriorated woman whose memory and intelligence were poor. She, of course, was incapable of performing all the tests described, but it is significant that she showed no greater disturbance in orientation after partial and after complete section of the corpus callosum than she showed before operation. For example, before operation she could not give a concise account of a movie she had seen, but became lost in circumstantial, petty details; after operation this defect remained as pronounced as before. Patient 2 showed slight clinical evidence of damage to the left cerebral hemisphere as a result of the brain abscess which was drained in 1937. This patient was of normal intelligence and was extremely cooperative, so that all tests were performed, with one exception. The exception was the cinema test—he never went to the movies because of the fear that he might have a seizure. However, he enjoyed reading stories and comprehended their content adequately. Similarly, serials and music over the radio were a source of enjoyment to him. Of those 5 patients (groups I-B-1 and I-B-2) with evidence of unilateral cerebral damage, the 3 (3, 4 and 5) with predominant involvement of the anterior portion of the cerebrum were all retarded mentally. Patient 4 had right cerebral palsy; patient 5 had had an "encephalitic" process at the age of 15 months, and in patient 3 probably a partial left middle cerebral artery infarct developed at 2 years of age. Of this group (group I-B-1) only patient 5 showed evidence of difficulty with orientation after operation, and this was temporary. She has been unable to perform the clock test with the left hand since operation. It is interesting to note that she presented sensory

changes (objective and subjective) in the left upper extremity, which suggests that added injury to the right hemisphere had occurred.

Patients 6 and 7 revealed clinical and laboratory evidence of damage to the posterior portion of the cerebrum (group I-B-2). This has been discussed in detail in a previous paper.[16] Patient 6 showed mild confusion and increased hostility for at least a week after operation. This hostility may well have been a result of his confusion. Subsequently no evidence of disorientation was noted. In patient 7 a cataleptoid state developed and she was confused for two weeks after operation. It is interesting that both these patients showed temporary, but definite, personality changes, in contrast to patients in group I-B-1.

In the patient (case 8) with evidence of diffuse involvement of the brain an evident mental decline and change of personality occurred after complete section of the corpus callosum. This patient's postoperative course was marked by frequent "terror spells," with loss of consciousness and the development of right hemiparesis. Consequently, it is impossible to evaluate the role of section of the corpus callosum alone in his clinical picture. One year later he still presented sensory disturbances in the right hand but was well oriented. The change in personality persisted; he was passive and quiet, in marked contrast to his preoperative status. How much of this personality change may have been due to a natural readjustment of adolescence is, of course, impossible to say.

In group II, consisting of 3 patients, evidence of postoperative cerebral damage was found. In the 2 patients (9 and 10) with partial section no obvious disorders of orientation were discernible. Patient 10, however, was not examined in detail. The case of patient 9 is interesting from several points of view. The partial section of the corpus callosum and the cerebral damage limited to the right frontal lobe did not result in any striking confusion during the "lucid" periods between his seizures. The inability to play the guitar was a result of the left hemiparesis. The loss of musical rhythm is unique, since other patients in this series did not show this phenomenon. Further sectioning of the corpus callosum produced no evidence of confusion.

Patient 11 showed, along with left hemiparesis, disturbances in sensorium for at least two weeks after her first operation, in which the body and the posterior half of the genu of the corpus callosum were sectioned. Her speaking of herself in the third person is probably a reaction best explained on a psychobiologic basis. She was uncomfortable, and a bit confused and worried, and it is not improbable that

16. Akelaitis, A. J.: Studies on the Corpus Callosum: V. Homonymous Defects for Color, Object and Letter Recognition (Homonymous Hemiamblyopia) Before and After Section of the Corpus Callosum, Arch. Neurol. & Psychiat. **48**: 108 (July) 1942.

she regressed temporarily to a childish level. The subsequent panic, with ideas of reference, and the severe depression were probably psychobiologic in origin. This introspective, frustrated, worrisome young woman had a reasonable fear that some day dementia paralytica would develop. It was only natural, therefore, that the hemiparesis and the frequent neurologic examinations resulted in a subjective realization of her fears and produced a panic. Similarly, the depression resulted in preoccupations, which, in turn, affected her memory, at least subjectively. It is usual for depressed patients to have a subjective feeling that their memory is impaired, but this cannot be demonstrated objectively. However, in this patient objective evidence of impairment of memory was present. Consequently, one is dealing with both neurogenic and psychobiologic factors. Subsequent section of the remainder of the corpus callosum had no effect on the psychobiologic picture. The depression lasted more than a year, and with its disappearance the patient returned to her preoperative status. With the clearing of the hemiparesis she successfully performed the clock test and was able to play the piano again.

Of the 10 patients belonging to group III-A, with normal neurologic signs and partial section of the corpus callosum, only 2, i. e., patients 12 and 18, were confused. In patient 12 the section was limited to the body of the corpus callosum, and the confusion was associated with numerous petit mal and grand mal seizures for the first two weeks after operation. Subsequently he showed no disorientation. The confusion shown by patient 18, most severe at night, was associated with an undetermined pyrexia, and on the disappearance of the fever the confusion cleared. It seems reasonable to conclude that the confusion of patient 12 was a result of anoxemia produced by the seizures and that confusion of patient 18 was a part of a nonspecific delirioid reaction. Consequently, in this group there is no evidence that partial section of the corpus callosum in patients with an essentially normal central nervous system results in disorientation. Further, it may be emphasized that no correlation exists between the extent of the callosal lesion and the degree of orientability. Moreover, 1 patient (21) undoubtedly had bilateral scarring of the tips of the frontal lobes and did not show any evidence of confusion after almost complete section of the corpus callosum.

In the 3 patients (22 to 24) belonging to group III-B-1, with severe hemiplegia, partial section of the corpus callosum produced no disorientation.

Patient 25 (group III-B-2), with evidence of unilateral involvement of the posterior portion of the cerebrum, after almost complete section of the corpus callosum showed a decided decline in mental ability. This was evident in the psychometric tests, the tendency to perseveration

and the impairment of memory. She has been unable to perform the clock test with her right hand since the operation. Although capable of writing with this hand, she has lost the ability to recognize forms and objects.

Patient 26 had Pick's atrophy and showed an organic type of reaction, with disturbances in sensorium, mental capacity and intellect. The corpus callosum was almost completely sectioned. The early postoperative course was stormy and was complicated by transitory right hemiplegia with aphasia. Subsequently, he returned to his preoperative status. This patient presented no conclusive evidence that the lesion of the corpus callosum actually resulted in accentuation of the preoperative organic reaction picture.

In brief, therefore, only 3 patients (6, 7 and 25) showed disorientation which may be directly attributed to section of the corpus callosum. The interesting common neurologic sign manifested by all 3 patients was the homonymous hemiamblyopia.[16] All 3 patients presented clinical and laboratory evidence pointing to a unilateral lesion in the parietooccipitotemporal region. With the exception of patient 25, this confusion was transient, lasting at most two weeks. It is also interesting that all 3 of the patients showed definite personality changes; patient 6 manifested exaggeration of hostility, patient 7 was cataleptoid and verbally unresponsive and patient 8 showed extreme perseveration. These psychobiologic reactions were probably the distinctive reaction of each patient to his or her state of confusion.

Study of cases 3, 7, 9, 11, 13, 18, 20 and 25 proves that section of the fornix together with partial or complete section of the corpus callosum has no greater effect on orientability than partial or complete section of the corpus callosum alone.

A study of those patients on whom lobectomy was performed before or after section of the corpus callosum discloses surprising facts. On patient 16, of group III-A, a right temporal lobectomy was performed two years before the callosal section. This combination of lesions produced no more effect than in the other patients (15, 19 and 20) of this group, in whom only a callosal section of the same or greater extent was present. In this case the "subordinate" temporal lobe was resected. In patient 10, of group II-A, a left occipital lobectomy was performed one year before the callosal section. Again, no disturbance in orientation occurred, although it must be emphasized that detailed studies were not made prior to the patient's death. Insofar as laterality studies can be utilized in the study of cerebral dominance, the "dominant" occipital lobe can be said to have been resected in patient 10. Case 3 is an example of the lack of any evidence of disorientation in a subject in whom right ("subordinate") frontal lobectomy was performed six months after complete section of the corpus callosum.

COMMENT

These observations suggest, therefore, that in certain persons partial or complete surgical section of the corpus callosum does not result in disorientation. This observation is contradictory to the evidence in the case studied by Trescher and Ford.[8] These authors were certain that the cerebral hemispheres were not damaged during the operation for the removal of a colloid cyst of the third ventricle. It is interesting to note, however, that their patient showed visual agnosia and alexia in the left homonymous visual field and tactile alexia in the left hand. In the patients of the present series, however, no such disturbances were found after complete section of the corpus callosum.[17] This observation suggests that the right hemisphere may have been damaged before operation, since these aspects are not mentioned as having been studied preoperatively, or the disturbances may have resulted from injury at operation. The work of Gamper [18] suggests that lesions in the periventricular region of the thalamus and the hypothalamus may be the pathologic substratum of the Korsakoff psychosis. Is it possible that in the removal of the tumor in Trescher and Ford's case these areas may have been sufficiently damaged to produce the extreme disorientation?

The following case illustrates this possibility.

J. W., a white bachelor aged 32, was admitted to the Strong Memorial Hospital May 12, 1941. At the age of 17, after a long run, transient left hemiplegia developed. At 31 right intracerebral hemorrhage occurred, and a large intracerebral clot was sucked out of the right parietal lobe. Left hemiplegia remained, grand mal seizures developed, which began with clonic movements on the hemiplegic side. On May 28 a craniotomy was performed and the corpus callosum sectioned in its entirety except for the last centimeter of the splenium. A puncture to the right of the midline at the point where the infundibulum joins the right mamillary body was made with the endotherm set at 5, the cutting current being used. In an effort to control bleeding, a tear in the floor of the anterior portion of the third ventricle was made accidentally.

The postoperative course was marked by a state of delirium, in which the patient was disoriented, delusional and emotionally unstable for one month. He had pyrexia, with the temperature up to 39 C. (102.2 F.) for one day after operation, but after this the temperature was normal. When seen in September 1941 he was well oriented, but according to his family his memory fluctuates considerably.

Thus in the case of this patient one has a good control. The corpus callosum was partially sectioned; the right hemisphere was damaged, and at operation the hypothalamus was injured. It is probable that the dis-

17. Akelaitis, A. J.: Studies on the Corpus Callosum: VII. Study of Language Functions (Tactile and Visual Lexia and Graphia) Unilaterally Following Section of the Corpus Callosum, to be published; footnote 10.

18. Gamper, E.: Zur Frage der Polioencephalitis haemorrhagica der chronischen Alkoholiker. Anatomischer Befunde beim alkoholischen Korsakow, und ihre Beziehung zum klinischen Bild, Deutsche Ztschr. f. Nervenh. **102**:122, 1928.

orientation resulted from the hypothalamic injury, since patients 3, 4 and 5, of group I-B-1, and patients 22, 23 and 24, of group III-B-1, with unilateral and predominantly anterior damage of the cerebrum before operation and partial or complete section of the corpus callosum, did not show confusion after operation. In this group only patient 5 had transient confusion for two days after operation, but this was mild.

None of the patients in this series showed the striking confusion which occurs in the early postoperative course of subjects with bilateral prefrontal leukotomy. Apparently, unilateral lesions in the anterior lobe of the cerebrum plus section of the corpus callosum do not result in disorientation, as seen in group I-B-1 (cases 3, 4 and 5) and group III-B-1 (cases 22, 23 and 24). Unilateral lesions in the posterior portion of the cerebrum plus section of the corpus callosum produced personality changes in all 3 patients of group I-B-2 (cases 6 and 7) and group III-B-2 (case 25), probably as an individual manifestation of their reaction to a transitory state of confusion. At no time, however, did they show confabulation, so characteristic of the Korsakoff syndrome.

It appears probable, to conclude from this study, that a pure lesion of the corpus callosum (partial or complete) does not result in disorientation. It can further be stated that, insofar as the present study indicates, partial or complete section of the corpus callosum in a patient with an old or a recent unilateral lesion of the frontal lobe produces no disorientation. Partial or complete section of the corpus callosum in a patient with an old unilateral lesion in the temporoparieto-occipital region produces a transitory state of confusion. Of the 3 cases reported here, the "subordinate" hemisphere was involved in case 7, mixed dominance was present in case 6 and the originally "dominant" hemisphere was damaged early in life in case 25. As Nielsen [19] has emphasized, however, there is no certainty that the occipital lobe dominant for object recognition is always in the left hemisphere in right-handed persons, and, consequently, it is impossible to be certain of the hemisphere "dominant" for visual functions in the cases reported here. In none of these 3 cases before operation was found the type of disorientation described by Brain.[20]

It is reasonable to assume that in those cases of tumor and vascular accident involving the corpus callosum in which disorientation and memory impairment are prominent symptoms, one is dealing with neighborhood or multiple effects. In the cases of thrombosis of the posterior cerebral arteries the disorientation that occurs is probably a

19. Nielsen, J. M.: Unilateral Cerebral Dominance as Related to Mind Blindness: Minimal Lesion Capable of Causing Visual Agnosia for Objects, Arch. Neurol. & Psychiat. **38**:108 (July) 1937.

20. Brain, W. R.: A Form of Visual Disorientation Resulting from Lesions of the Right Cerebral Hemisphere, Proc. Roy. Soc. Med. **34**:771, 1941.

result of bilateral lesions of the occipital lobes, as suggested by Hartmann.[21] In cases of tumor one is dealing not alone with involvement of the hemispheres but in some instances with disturbance of function of the hypothalamus, which, in turn, may produce disturbances in orientability. It is to be emphasized that in these so-called experiments of nature one is not dealing with a cleancut lesion but is concerned with a general picture involving the phenomenon of diachisis of von Monakow,[22] and probably other physiologic factors, of which at present there is little knowledge.

SUMMARY AND CONCLUSIONS

In 26 cases of epilepsy orientation was studied before and after operation, in which the corpus callosum was sectioned partially or completely.

In group I, made up of 8 cases, the corpus callosum was sectioned completely. In the 2 cases in which the neurologic signs were normal (group I-A) no evidence of disorientation was present after operation. Group I-B consisted of 3 cases in which the anterior portion of the cerebrum was predominantly involved unilaterally and no disorientation was present after operation (group I-B-1) and 2 cases in which the posterior portion of the cerebrum was predominantly involved unilaterally and a temporary state of disorientation occurred after operation (group I-B-2). The patient (case 8) with diffuse involvement of the brain showed a decline in mental ability and a change in personality after operation (group I-C). However, the postoperative course was complicated by the development of "terror spells" and right hemiparesis, and it is impossible to evaluate the role of the callosal section alone. It seems justifiable to conclude that complete section of the corpus callosum may produce a temporary state of disorientation in patients with unilateral involvement of the posterior portion of the cerebrum. In the 2 cases in this study (cases 6 and 7) the lesions were in the right parieto-occipitotemporal region. Ambilaterality was present in case 6 and strong right handedness and right footedness in case 7.

In group II, made up of 3 cases, with partial section of the corpus callosum and evidence of postoperative damage to the right, or subordinate hemisphere, namely, acute and simultaneous lesions, temporary disturbances in sensorium were observed in only 1 instance (case 11). Psychobiologic factors probably accentuated this difficulty. Subsequent completion of the callosal section, did not aggravate the disturbance in concentration and memory for recent events. The anterior portion of the right cerebrum was predominantly involved in all 3 cases.

21. Hartmann, F.: Die Orientierung, Leipzig, F. C. W. Vogel, 1902.
22. von Monakow, C.: Gehirnpathologie, Vienna, A. Hölder, 1905.

In group III, made up of 15 cases, the section of the corpus callosum varied in degree, the minimal division involving the body (case 12) and the maximal division including almost the entire corpus callosum except for a few fibers in the tip of the splenium. In all 10 cases in which neurologic signs were normal (group III-A) and in 3 cases in which unilateral involvement of the anterior portion of the cerebrum was evident (group II-B-1) orientation remained intact after operation. The patient in case 25 (group III-B-2), with damage to the once dominant left hemisphere and with evidence of greatest injury to the left parietal region, showed confusion after almost complete section of the corpus callosum. The difficulty in sensorium consisted of preservation, memory defects and inability to perform the clock test with the right, or hemiplegic, hand. The patient in case 26, with diffuse involvement of the brain, probably Pick's atrophy, had a stormy postoperative course with complications, but when examined two and five months after operation he showed no greater disturbances in sensorium and mental capacity than before operation. It seems reasonable to conclude that partial section of the corpus callosum may result in a temporary state of disorientation in patients with a unilateral lesion of the posterior portion of the cerebrum.

Apparently, section of the fornix along with partial or complete section of the corpus callosum has no greater effect on orientability than partial or complete section of the corpus callosum alone.

The conclusion seems warranted, therefore, that partial or complete section of the corpus callosum results in temporary confusion only if unilateral involvement of the posterior portion of the right or left hemisphere coexists.

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REMOVAL OF MALIGNANT THYMOMA IN A CASE OF MYASTHENIA GRAVIS

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Medical therapy of some of the less common diseases is occasionally based on uncertain premises. Such is the thin thread of evidence that forms the rationale for removal of thymic tumors in cases of myasthenia gravis. So rare are recorded instances of successful removal of a tumor of the thymus from a patient suffering from myasthenia gravis that there is yet no conclusive evidence of the value of this procedure.

Interest in the relation of myasthenia gravis to activity of the thymus was first stimulated by the report of Weigert [1] in 1901. He described the observation, at autopsy, of a thymic tumor in a patient who had died of myasthenia gravis. A series of 56 cases of the disease with autopsy were collected by Bell [2] in 1917. Of this group, enlargement or tumor of the thymus was present in almost 50 per cent. Holmes [3] related, in 1923, that in 6 of 8 cases of myasthenia gravis in which he had performed autopsy he had observed either enlargement or tumor of the thymus. Aronson,[4] in a review of the literature up to August 1940, found a total of 89 cases of myasthenia gravis with autopsy, in 48 per cent of which "a lesion of the thymus gland was the outstanding feature." It is likely that cases are more apt to be reported in which gross hypertrophy or tumor of the thymus is apparent at autopsy. This tendency may be balanced by one's frequent failure to note microscopic tumors or abnormal remnants of thymic tissue unless a thorough exploration of mediastinal fat is undertaken. Nevertheless, occasionally even the most

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1. Weigert, C.: Pathologisch-anatomischer Beitrag zur Erb'schen Krankheit, Neurol. Centralbl. **20**:597, 1901.

2. Bell, E. T.: Tumours of the Thymus in Myasthenia Gravis, J. Nerv. & Ment. Dis. **45**:130, 1917.

3. Holmes, G., in discussion on Mott, F. W., and Barrada, Y. A.: Pathological Findings in the Central Nervous System of a Case of Myasthenia Gravis, Brain **46**:237, 1923.

4. Aronson, S. F.: Myasthenia Gravis: A Discussion, with Presentation of a Case Associated with a Thymoma, Ann. Int. Med. **15**:137, 1941.

thorough search of the mediastinum fails to disclose one shred of thymic tissue in a patient who has died of myasthenia gravis.

There have been scattered reports of successful or partial removal of the thymus gland, with variable effects on the disease. Sauerbruch, cited by Schumaker and Roth,[5] removed a hypertrophied thymus in a young woman who suffered from myasthenia gravis and hyperthyroidism. He had ligated the right superior thyroid artery and vein a few weeks before thymectomy, without relieving the hyperthyroidism. After thymectomy there was decided improvement of both the myasthenia and the hyperthyroidism. Sixteen months later an exacerbation of the hyperthyroidism necessitated subtotal thyroidectomy. Apparently the myasthenic symptoms had disappeared by this time. Von Haberer[6] treated by thymectomy a 27 year old man who was suffering from myasthenia gravis and stated that three years later there was much improvement. Leriche and Jung[7] reported their experience in the case of a 16 year old girl who had suffered from myasthenia gravis since early childhood. They performed thymectomy, removing a 16 Gm. gland of infantile type. Two months later the myasthenia gravis was apparently unchanged.

The first well controlled group of cases in which thymectomy for myasthenia gravis was performed is described in a recent preliminary report by Blalock and his associates,[8] at Johns Hopkins Hospital. They removed every available remnant of the thymus gland in 6 cases of myasthenia gravis. In 3 of their cases the results a few months later appeared to be successful.

Few operations for the removal of thymic tumor in a patient suffering from myasthenia gravis have been reported, and there appear to be only 4 records of patients who survived the operation. Blalock, Mason, Morgan and Riven,[9] in 1939, removed an anterior mediastinal tumor in a woman aged 20 who had suffered from myasthenia gravis periodically for four years. A roentgenogram of the chest had revealed a tumor, and she had been given courses of roentgen therapy. When operation was performed the disease was in a state of remission. The

5. Schumaker and Roth: Thymektomie bei einen Fall von Morbus Basedowii mit Myasthenia, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**:746, 1913.

6. von Haberer, H.: Zur klinischer Bedeutung der Thymusdruse, Arch. f. klin. Chir. **109**:193, 1917.

7. Leriche, R., and Jung, A.: Thymectomie dans un cas de myasthénie, Mém. Acad. de chir. **65**:334, 1939.

8. Blalock, A.; Harvey, A.; Ford, F., and Lilienthal, J. L.: The Treatment of Myasthenia Gravis by Removal of Thymus Gland, J. A. M. A. **117**:1529 (Nov. 1) 1941.

9. Blalock, A.; Mason, M. F.; Morgan, H. J., and Riven, S. S.: Myasthenia Gravis and Tumours of the Thymic Region, Ann. Surg. **110**:544, 1939.

rounded, encapsulated mass which was removed did not contain any neoplastic cells but was considered to represent the remains of a necrotic thymic tumor. The patient had one mild relapse during the first ten months after operation but thereafter remained normal up to the time of the authors' report, four years later.

Campbell, Fradkin and Lipetz [10] in 1939 removed a thymic tumor from a 45 year old woman who had suffered from a severe form of myasthenia gravis for seven months prior to operation. The disease had not responded to roentgen therapy and was in an active stage at the time of operation. The tumor was benign. After operation there was considerable improvement in the myasthenic symptoms, but it was difficult to judge whether this result should be attributed to removal of the thymoma or to a partial spontaneous remission.

Eaton [11] has recently referred briefly to a case of myasthenia gravis in which Clagett successfully removed a thymoma at the Mayo Clinic in 1941. The operation was performed while the disease was in a remission, which began two months after roentgen therapy of the tumor. Two months after operation there had been no recurrence of symptoms.

In August 1941 Poer [12] performed the first successful operation for removal of carcinoma of the thymus in a patient with myasthenia gravis. A man of 52 had suffered from characteristic myasthenia gravis with remissions for two years prior to operation. The disease was well advanced and active at the time of operation. Microscopic examination of the tumor proved it to be a typical carcinoma of the thymus. The patient made a remarkable recovery and five months after operation was back at work, without any symptoms of myasthenia and requiring no treatment.

REPORT OF CASE

History and Examination.—J. B., a woman aged 29, a clerk, who was referred by Dr. Alan Anthony, of Vancouver, was first seen in May 1940, with complaints of double vision, drooping eyelids and difficulty with swallowing and speaking. Her past and family histories were not significant. The present illness commenced insidiously in March 1940 and had progressed slowly.

She was an alert, intelligent, slightly obese woman, with a good complexion. The general physical examination, including a Kahn test of the blood, revealed nothing significant. There was bilateral ptosis, most pronounced on the left side. All movements of the left eyeball were slightly impaired, and external rotation of the right eyeball was almost nil. She had diplopia on looking in any direction. The pupils were large and reacted well to light, but this reaction tended to tire

10. Campbell, E.; Fradkin, N. F., and Lipetz, B.: Myasthenia Gravis Treated by Excision of Thymic Tumour, Arch. Neurol. & Psychiat. **47**:645 (April) 1942.

11. Eaton, L. M.: Myasthenia Gravis: Its Treatment and Relation to the Thymus, Proc. Staff Meet., Mayo Clin. **17**:81, 1942.

12. Poer, D. H.: Effect of Removal of Malignant Thymic Tumour in a Case of Myasthenia Gravis, Ann. Surg. **115**:586, 1942.

with successive stimulation. There was some generalized loss of facial expression, with weakness in closing the eyelids and showing her teeth. Speech had a nasal quality, and as she spoke she supported her chin with her hand. She could not close her mouth against even very slight resistance. The palate did not elevate well. Neurologic examination was otherwise negative. The picture was typical of myasthenia gravis.

Intramuscular injection of 2 cc. of prostigmine methylsulfate caused remarkable improvement. The ptosis cleared up on the left side, and the right upper eyelid was raised above its normal position. Diplopia on forward gaze disappeared, and she regained ability to close her jaws tightly.

Roentgenograms of her chest, taken by Dr. W. A. Whitelaw, demonstrated an oval shadow 2½ inches (6.4 cm.) in length in the anterior mediastinum, which moved synchronously with the cardiac pulsation. It presented the appearance of a tumor, to which the cardiac pulsations were transmitted.

Clinical Course.—Treatment was started with ephedrine hydrochloride, ¾ grain (0.048 Gm.) twice a day, and gelatin powder, ½ ounce (15.5 Gm.) daily. Prostigmine bromide by mouth was tried on a few occasions, but economic considerations at this stage precluded an adequate trial of this therapy.

In August 1940, she was given a course of ten daily roentgen irradiations under the direction of Dr. B. J. Harrison, of the department of roentgenology of the Vancouver General Hospital. The estimated total dose received by the thymus area was 88 per cent of 3,000 r. No immediate benefit was noted after irradiation therapy. She remained in bed at home for four months. During this time she had several severe choking spells, which were relieved at once by intramuscular injection of prostigmine methylsulfate. In December 1940 she began getting up for a few hours daily. She still had occasional mild choking spells and usually had some ptosis by evening. The diplopia had cleared up, and her voice was normal. During the spring and summer of 1941 she made further improvement but was still not fit for work. In September 1941, she commenced part time work as clerk in a store. Within a few weeks difficulty with swallowing and speaking returned, and for the first time she noted marked weakness of her arms, particularly of her grip. She started to take 4 to 5 tablets of prostigmine bromide, 15 mg. each, in addition to the ephedrine hydrochloride, ¾ grain twice a day, and the gelatin powder. The situation improved, but she was rarely able to do a full day's work.

Roentgenograms of her chest in October 1941 (fig. 1) disclosed slight enlargement of the tumor. In view of her lack of response to irradiation and medicinal therapy and the roentgen evidence of progressive enlargement of the tumor in the anterior mediastinum, surgical removal of the tumor appeared to be indicated.

On Jan. 22, 1942, with the assistance of Dr. W. E. Harrison, the tumor was successfully removed. The technic of operation, as well as the preoperative and postoperative care, was planned to follow closely the instructions of Blalock and associates. She was admitted to the hospital two days before operation, and immediate administration of sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine), 30 grains (1.95 Gm.) for two doses and then 15 grains (0.98 Gm.) every four hours, was begun. Her usual dose of prostigmine bromide and other drugs was continued until the morning of operation, when she received 1/100 grain (0.6 mg.) of atropine sulfate, ⅙ grain (0.010 Gm.) of morphine sulfate and 3 cc. of prostigmine methylsulfate intramuscularly.

Anesthesia was induced (Dr. D. Freeze) with ethyl chloride, followed by administration of ether and oxygen through a Magill intratracheal tube. The pharynx around the tube was packed with 2 inch (5 cm.) gauze. Her progress

during anesthesia was placid, with little variation of the pulse rate above the 80's and an even respiratory rate of 30 per minute. The operation took three and one-half hours. During its course she received 1,000 cc. of 5 per cent dextrose and saline solution and 400 cc. of blood. At the end of the second hour she was given 2 cc. of prostigmine methylsulfate intramuscularly. With the sternum split down to the fourth rib and widely retracted, an excellent view of the tumor was obtained. It proved to have a tough capsule, which facilitated better exposure by traction sutures. Several times it was noted that strong traction on the tumor caused temporary irregularity of the cardiac rhythm. One fair-sized vein which

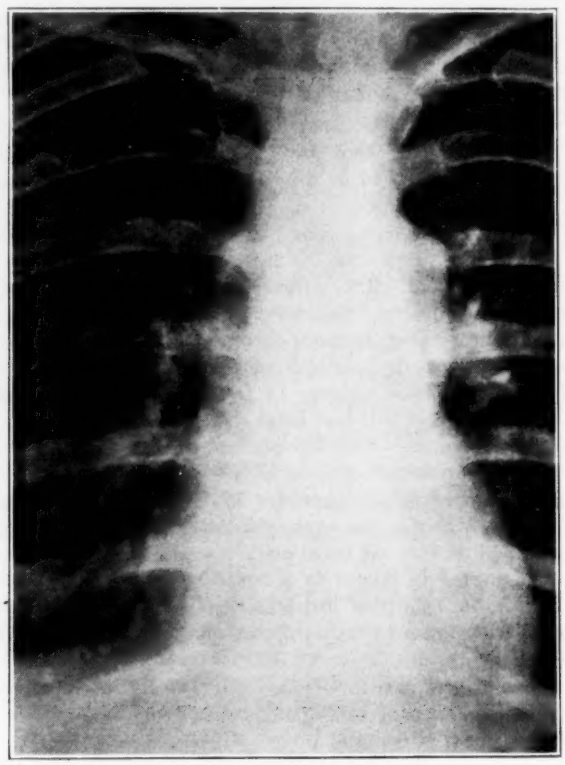

Fig. 1.—Anteroposterior roentgenogram of chest, showing tumor in the upper portion of the mediastinum.

emerged from the lower pole of the tumor was divided between silk ligatures. No other vascular connections of note were encountered. Cleavage from surrounding tissues was easily established on the right side, but on the left side separation was more difficult and a long tear was made in the pleura. Collapse of the lung on this side had no untoward effect on the patient. After removal of the tumor no trace of thymic tissue could be seen. Fearing that air might be forced into the anterior mediastinum in large quantities from the left pleural sac after operation, we filled the entire left pleural cavity with warm physiologic solution of sodium chloride and then closed the pleura under saline solution.

Mopping up the anterior mediastinum demonstrated that this closure was watertight. The divided sternum was approximated by two heavy braided silk sutures and the subcutaneous tissue and skin by interrupted silk sutures without drainage. While the closure was being completed a needle attached to a pneumothorax outfit was introduced into the left pleural cavity in the axilla and the saline solution withdrawn, allowing reexpansion of the lung.

Pathologic Report (Dr. H. H. Pitts).—The specimen (fig. 2) consisted of a pyriform, well circumscribed, somewhat boggy structure, measuring 7.5 by 4 by 2.5 cm. and weighing 30 Gm. On section it presented a somewhat bilocular appearance, the upper locule containing yellowish, custard-like material, while the lower portion showed a pinkish gray, homogeneous growth partially surrounded by a cystic space. Microscopic sections of the upper portion showed a degenerated amorphous material with scattered fatty acid crystals and no cellular elements. Sections through the homogeneous lower pole (fig. 3) revealed a diffuse cellular process characterized

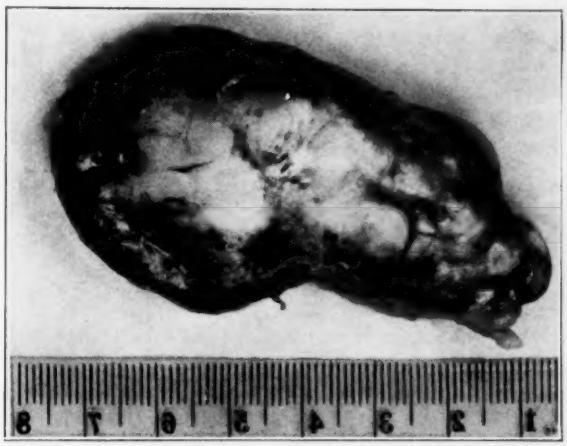

Fig. 2.—Photograph of the tumor.

by large and small cells of lymphocytic type, which stained deeply and varied greatly in size and shape, with occasional mitotic figures and a few multinuclear cells. Scattered throughout were large, pale epithelial cells and degenerated thymic corpuscles. A very thick, semihyaline capsule surrounded the growth.

The growth was diagnosed as a malignant thymic tumor of lymphosarcoma type.

Prof. William Boyd, of Toronto, Canada, examined the slides and agreed that it was a thymic tumor. He stated that it was identical with the description of "thymoma" in Ewing's [13] classification of thymic tumors.

Postoperative Course.—The patient was given 3 cc. of prostigmine methyl sulfate every three hours and atropine sulfate $\frac{1}{150}$ grain (0.4 mg.), every four hours. The afternoon following operation she received two doses of sodium sulfathiazole (sodium salt of 2-[paraaminobnezenesulfonamido]-thiazole) intravenously, and the following day administration of sulfadiazine, 15 grains (0.98 Gm.) every four hours, was begun. Fluids were given only intravenously for twenty-four hours. Nurses

13. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, p. 1002.

were instructed to see that the patient coughed deeply every hour during the day and every two hours during the night and to support her chest with their hands to prevent pain. Respirations were rapid and labored the first day but gradually became normal. Daily roentgenograms of the chest for the first four days disclosed nothing of note. Her temperature was normal by the fourth postoperative day. Her only complaint at this time was of abdominal cramps, which were thought to be due to the prostigmine. Prostigmine bromide by mouth was started on the second postoperative day in doses of 45 mg. every three hours, and the amount was gradually reduced to 15 mg. every three hours by the fourth day. On the fourth and fifth days she had some visual hallucinations and noted occasional twitching of muscles in the neck and arms. She was discharged from the hospital three weeks after operation. At this time she was taking four doses of prostigmine

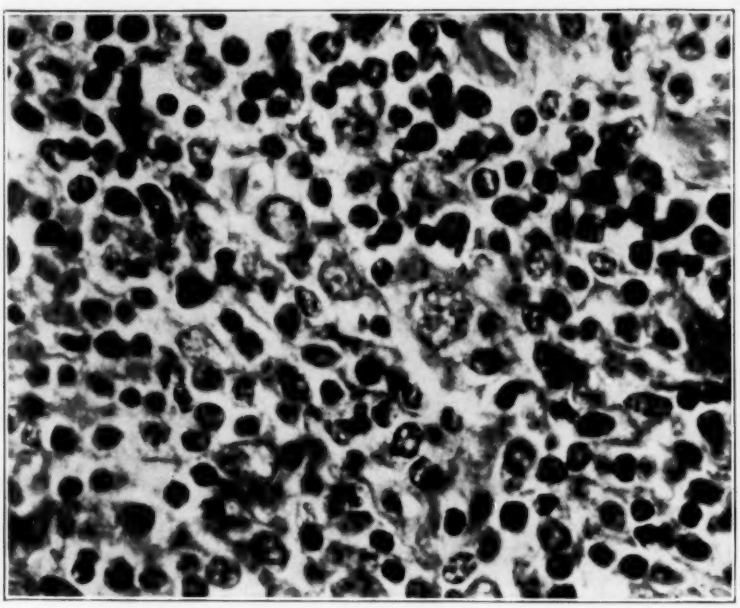

Fig. 3.—Photomicrograph of the tumor. Hematoxylin and eosin; × 510.

bromide, 15 mg. each, and two doses of ephedrine hydrochloride, ¾ grain (0.045 Gm.), daily. She was able to be out of bed for several hours daily and appeared to be practically symptom free.

Five weeks after operation she was able to carry on normal activities at home with only 2 tablets, 15 mg. each, of prostigmine bromide daily, in addition to ephedrine. When next seen on March 8 she was again much worse. The situation was practically the same as at the first examination, in 1940. On April 2 she started increasing the number of tablets of prostigmine bromide and gradually reached a dose of 11 to 15 tablets per twenty-four hours, taken at intervals of one to one and a half hours. Her eyes improved, but swallowing and the use of her arms were not much better. On April 15 a cold in the head developed, and her symptoms were so aggravated that she had to be readmitted to the hospital.

At present (May 9), four months after operation, she is ready to leave the hospital again, but is not free of myasthenic symptoms, in spite of the use of

prostigmine bromide, 15 mg. every two hours day and night, and ephedrine hydrochloride, ¾ grain twice a day.

COMMENT

Medical literature dealing with the treatment of myasthenia gravis by removal of the thymus gland or a thymic tumor is meager at present. Judging from the reports to date, the results of thymectomy seem to be more promising than those of removal of thymic tumor. To arrive at any conclusions regarding the etiology and treatment of myasthenia gravis from these operations, it appears advisable to distinguish sharply between cases in which thymectomy was done and those in which thymic tumor was removed.

When more cases of successful removal of thymic tumor have been recorded, it is likely that the pathologic type of tumor will be found to be important, i. e., whether the tumor is lymphosarcoma (thymoma) or carcinoma. It is noteworthy that of the 5 recorded cases of successful removal of thymic tumor (including my own), the only one [12] in which dramatic and immediate cure resulted was the single instance of carcinoma in the series. In 2 of the remaining 4 cases [14] the tumor was a lymphosarcoma, and in both it is open to question whether operation caused improvement or prolonged a remission. In the third case [9] it seems futile to argue that operation might have affected the disease when the tumor that was removed was entirely devoid of anything but debris and fibrous tissue, whatever its origin might have been. In my own case, removal of a lymphosarcoma did not have any appreciable effect on the myasthenia gravis.

SUMMARY

A case of myasthenia gravis associated with malignant thymoma is reported. Successful removal of the thymic tumor did not result in any improvement of the myasthenia gravis.

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14. Campbell, Fradkin and Lipetz.[10] Eaton.[11]

CONVULSIONS IN NONEPILEPTIC PATIENTS ON WITHDRAWAL OF BARBITURATES, ALCOHOL AND OTHER DRUGS

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Convulsions in nonepileptic persons after sudden withdrawal of hypnotic drugs are relatively unknown. Experience with 7 patients observed almost simultaneously has the value of an experiment and gives the starting point for a more systematic discussion of "withdrawal seizures."

The 7 patients whose cases are described here belonged to a group of 50 or 60 very disturbed patients in Pilgrim State Hospital who had been kept under continuous sedation with soluble barbital U. S. P. for months or years, as reported by Polatin.[1] Treatment of chronically disturbed patients with mental disease by prolonged use of sedatives, such as bromides and barbiturates, has been recommended by various authors; no narcotic but merely a sedative effect is desired in such treatment. To these patients soluble barbital (sodium barbital, or sodium diethylbarbiturate) was given in aqueous solution, the average dose being 20 to 30 grains (1.3 to 1.95 Gm.) daily. In April 1939, owing to a shortage in the supply of the drug, the patients were completely deprived of the barbiturate to which they had become accustomed over a period of a year and a half or longer. Four or five days after this sudden withdrawal 7 patients had generalized convulsions. Other unknown causes could be excluded because the drug was withdrawn on different days from different patients, but the convulsions always occurred after the same interval of four or five days after withdrawal. As the histories of all these patients are essentially the same, it is sufficient to describe briefly 1 of them.

CASE 1.—S. F., aged 25, had a condition diagnosed as dementia praecox. The family and his own history were negative for epilepsy. At the age of 16 ideas of being poisoned and persecuted and loss of emotional display were present. He was committed to a state hospital in 1934, since when he has been disturbed most of the time. In September 1937 medication with soluble barbital U. S. P. was initiated, and an average daily dose of between 20 and 30 grains (1.3 to 1.9 Gm.) was given continuously for the following nineteen months.

From the Pilgrim State Hospital, Brentwood, N. Y.

1. Polatin, P.: Prolonged Sedation with Sodium Barbital, of Male Disturbed Continued Treatment Patients, Psychiatric Quart. **11**:213, 1937.

On April 17, 1939, at 8 p. m., he had the last medication. On April 21, at 6:40 p. m., a generalized epileptic seizure occurred. During the following three years of observation no further convulsion occurred, although no anticonvulsive medication, except for occasional sedatives, was given.

On Feb. 15, 1942 an electroencephalographic record showed normal activity, no slow waves or irregularities and no abnormal waves during hyperventilation.

None of the other 6 patients had had convulsions before, and all had a negative family history for convulsions except 1, whose mother apparently died of a brain tumor with seizures. The convulsions occurred in all cases on the fourth or fifth day after discontinuance of soluble barbital. Since this occurrence all of these patients have been under constant hospital observation for a period of three years, during which no further epileptic phenomena have been noted. Electroencephalograms made on 2 patients showed normal patterns; the other 5 patients were too disturbed and uncooperative to have records taken.

This clinical experience presented several problems. Epileptic seizures due to intoxication with barbiturates could hardly be expected, since not only has the anticonvulsive effect of all barbiturates been shown experimentally but the drugs have all been tried on epileptic patients. The superiority of phenobarbital over the other barbiturates is due only to the combination with a phenyl group.[2] The characteristic narcotic effect of all barbiturates seems to determine the withdrawal seizures which occur equally with all of them, as will be seen later. The premise for the occurrence of these convulsions is the chronic use of the drug prior to withdrawal.

In the literature on so-called withdrawal psychoses after barbiturate addiction epileptic seizures are mentioned frequently [3] as occurring before or during these psychotic syndromes, which represent a delirium-like picture starting a few days after withdrawal of the barbiturate. Epileptic seizures following barbital addiction occur six to ten days after withdrawal of the drug, the interval between the withdrawal and the seizure being longer after barbital intoxication than in my cases, in which the sodium salt of barbital (soluble barbital U. S. P.) was used. Single cases have been reported in which convulsions followed withdrawal of other barbiturates.

Of special interest are convulsions occurring after withdrawal of phenobarbital, the anticonvulsive action of which is widely recognized. Addiction to phenobarbital in nonepileptic persons is rare; however,

2. Putnam, T. J., and Merritt, H. H.: Chemistry of Anticonvulsant Drugs, Arch. Neurol. & Psychiat. **45**:505 (March) 1941.

3. (*a*) von Muralt, K.: Ein Fall von akuter Psychose bei chronischer Trional-Veronal-Vergiftung, Ztschr. f. d. ges. Neurol. u. Psychiat. **22**:122, 1914. (*b*) Pohlisch, K.: Ueber psychische Reaktionsformen bei Arzneimittelvergiftungen, Monatschr. f. Psychiat. u. Neurol. **69**:200, 1928. (*c*) Kraepelin, E.: Delirien, Halluzinose und Dauervergiftung, ibid. **54**:43, 1923.

Pohlisch [3b] described the case of a nonepileptic addict who, nine days after withdrawal, had four epileptic convulsions and a delirium of three days' duration.

This brings up for consideration experiences with the most frequent type of phenobarbital addicts, namely, epileptic patients who have been treated with the drug. Status epilepticus after sudden withdrawal of phenobarbital is a well known occurrence. Grinker,[4] Fox [5] and others demonstrated conclusively that seizures in epileptic patients not only increased in number when phenobarbital was stopped but became much more frequent than they had been prior to any medication.[5] Schmidt,[6] trying to show that phenobarbital may lose its effect after use for years, reported the case of an epileptic patient who had seizures every six weeks; two days after sudden discontinuance of phenobarbital medication he began to have several fits daily for approximately a week, after which period the seizures occurred again at the usual six week intervals. Withdrawal seizures in nonepileptic patients, as described in this paper, make it probable that this increased number of fits in epileptic persons is not explained merely by deprivation of their anticonvulsive medication, but that an additional mechanism with convulsive effect in itself must be suspected. This becomes still more probable when one considers that status epilepticus after discontinuance of bromide medication was rare. The danger of status epilepticus after sudden withdrawal of medication was less known when bromides were used exclusively.

The cases cited so far have been exclusively those of seizures following the chronic use of barbiturates. It is striking that in spite of the frequency of acute intoxication produced by barbiturates as a means of suicide (Hambourger [7]) no cases of convulsions following the comatose state have been reported.

Intermediate between acute and chronic intoxication is the condition of prolonged narcosis therapy, as introduced by Klaesi in the treatment of mental disorders, in which large doses of barbiturates, chloral hydrate or paraldehyde are given for ten to twenty days. The literature on this type of therapy contains only rare reports of convulsions several days after discontinuance of somnifaine (a mixture of the diethylamine salts of diethylbarbituric acid and allylisopropylbarbituric acid), sodium

4. Grinker, R. R.: The Proper Use of Phenobarbital in the Treatment of the Epilepsies, J. A. M. A. **93**:1218 (Oct. 19) 1929.

5. Fox, J. T.: Luminal-Sodium in the Treatment of Epilepsy, Lancet **2**:589, 1927.

6. Schmidt, G.: Erscheinungen bei Luminalentziehung, München. med. Wchnschr. **85**:1944, 1938.

7. Hambourger, W. E.: The Promiscuous Use of the Barbiturates: Analysis of Hospital Data, J. A. M. A. **114**:2015 (May 18) 1940.

amytal or other drugs.[8] Merloo[9] saw a convulsion in only 1 of 500 patients treated with prolonged sleep. Occasional reports of twitchings and tonic-clonic movements not after but during the narcosis[10] obviously indicate another mechanism. A survey of the large Swiss literature on the subject revealed no case of epileptic seizures, perhaps because of the slower withdrawal of the narcotic. In summary, therefore, it can be stated that seizures from withdrawal of barbiturates do not occur after acute intoxication, appear seldom after short use of even very large doses, as in narcosis treatment, but are frequent after withdrawal following chronic addiction.

Barbiturates are not the only drugs which produce withdrawal convulsions. Two instances of convulsions after withdrawal of chloral hydrate, one of the oldest known hypnotics of the alcohol group, are to be found in the older literature.[3b] Of greater importance is the occurrence of convulsions after the use of another hypnotic, paraldehyde. Although addiction to paraldehyde is infrequent, the proportion of withdrawal seizures seems to be high.[3b] They are associated with delirium-like psychotic episodes. The first case was described by von Krafft-Ebing[11] in 1887. Drug addicts often take several varieties simultaneously, as did a patient of Nothass,[12] who, after use of paraldehyde, barbital and phenobarbital, went into status epilepticus on the second day after sudden withdrawal of the drugs. In none of the aforementioned cases had epileptic seizures ever occurred before deprivation of the drug.

The simultaneous occurrence of convulsions and delirium in cases of paraldehyde addiction brings up the question of epileptic seizures and delirium in alcoholism. All observers of patients during withdrawal of paraldehyde have mentioned the similarity between the delirium of these patients and the delirium tremens of alcohol addicts. The delirium of both is frequently associated with epileptic seizures. Paraldehyde, as well as the other drugs discussed here, is a hypnotic of the group of aliphatic alcohols and aldehydes and is closely related to the most frequently used alcohol, ethyl alcohol. It is well known that alcohol in large doses has the effect of a narcotic. This action is still being used to advantage among native people for operative

8. Parfitt, D. N.: Treatment of Psychoses by Prolonged Narcosis, Lancet **1**:424, 1936. Broder, S. B.: Sleep Induced by Sodium Amytal, an Abridged Method for Use in Mental Illness, Am. J. Psychiat. **93**:57, 1936.

9. Merloo, A. M.: Action of Barbituric Acid Compounds, J. Ment. Sc. **79**: 336, 1933.

10. Palmer, H. D., and Braceland, F. J.: Six Years' Experience with Narcosis Therapy in Psychiatry, Am. J. Psychiat. **94**:37, 1937.

11. von Krafft-Ebing, R.: Ueber Paraldehyd-Gebrauch und Missbrauch, nebst einem Falle von Paraldehyd-Delirium, Therap. Monatsh., 1887, p. 244.

12. Nothass: Paraldehydpsychosen, Allg. Ztschr. f. Psychiat. **76**:826, 1920.

procedures. However, not only theoretic considerations but several observations, especially those in the following 2 cases, suggested the analogous concept of epileptic seizures in alcoholic patients as a withdrawal symptom.

CASE 2.—E. M., a white man aged 30, whose father was alcoholic, had no personal history of convulsions until the age of 25. At this time he married and shortly afterward started drinking heavily. Some time later he had his first fit, after consuming an excessive amount of alcohol. The fits were described as typical epileptic seizures. They repeated themselves at varying intervals of weeks or months, but occurred exclusively after the taking of large amounts of alcohol. His account of the relation between drinking and the fits was fully corroborated independently by his wife and his brother. They stated that whenever he took alcohol he had severe stomach trouble. He usually started drinking before supper and went on drinking for several hours, but came home regularly before midnight because of abdominal pain, nausea and sometimes vomiting. The day after such an alcoholic excess he could not drink or eat. In the afternoon or during the following night he would have an epileptic convulsion. The relation between drinking and the fits was especially clear because of his stomach trouble, which stopped his drinking regularly and abruptly after a few hours. Convulsions occurred after abstinence from alcohol for fifteen to twenty hours. He never had two fits on the same day, and no convulsions occurred at times when he did not drink. In December 1940 he had what was described as delirium, with optic and haptic hallucinations for several days. Later, a convulsion with subsequent confusion led to his admission to Bellevue Hospital, on Jan. 31, 1941. From there he was committed to Pilgrim State Hospital, where he neither showed the mental symptoms of epilepsy, nor had any convulsions.

Electroencephalograms, taken on July 24, 1941, showed normal activity except for slight irregularity of wave form.

CASE 3.—A. S., a man aged 35, had a negative family and personal history for epilepsy. In 1932 he began to drink. Whenever he drank he was unable to eat.

In December 1940 his relatives kept him at home for several days without alcohol. During this time, at the age of 35, he had his first convulsion. The following night he began to have visual and haptic hallucinations and consequently was admitted to Pilgrim State Hospital with the diagnosis of delirium tremens. The mental picture cleared up the same day, and he was paroled later.

On May 6, 1942, in the evening, he was returned from parole because he had taken up his drinking habit again. At this time he was at work and had been without alcohol for at least twelve hours. He was sober, had no odor of alcohol and was quiet and cooperative and showed no mental symptoms. On May 7, at 7:30 a. m., more than twenty-four hours after his last drink, he had a generalized seizure. A second generalized convulsion followed at 10 a. m. On May 8, at 7 a. m., he had a third convulsion. In the afternoon of this day he became confused, picked at his clothes, tried to fix an imaginary necktie and put on the bed sheets as pants. He said later that he saw a mouse running along the wall and that he had had visual and hepatic hallucinations of spiders and bugs. The face and eyes were reddened, and he was trembling and sweating. He was treated with lumbar puncture and given dextrose and paraldehyde. Under this therapy he began to sleep. On May 11 he awoke and was in good mental condition.

There are two groups of patients whose convulsions are correlated with addiction to alcohol. The first group consists of epileptic patients who have had fits before they ever drank but who are especially likely to have convulsions after an alcoholic excess. The condition in the second group, of which case 2 is a typical representative, is rare. It has been called "alcohol epilepsy" in a stricter sense by older clinicians and disputed as a disease entity. Patients in this group have epileptic seizures only after alcoholic abuse, never without it. Certainly, this condition is not a disease in itself, and a specific tendency to seizures must be accepted in these patients as well, but the special interest in their convulsions lies in the fact that they may offer the clue to an understanding of the influence of alcohol on increase in seizures in all epileptic persons. In the case cited the seizures never occurred while the toxic effects of the alcohol itself were present, but were present only at those times when most or all of the alcohol was supposedly burnt. A review of the rather scant literature on alcohol epilepsy revealed the statement of the French psychiatrist Féré[13] that in the Bicêtre the patient with this type of convulsions had seizures only the day after return from a vacation. Müller,[14] in his systematic study of the subject, stated likewise that such patients had fits only on Mondays, after their return to the hospital; the fits never occurred in saloons or on the street. Cobb, Christian and Lennox[15] also mentioned that seizures usually occur during the sobering-up process.

There is, obviously, no other cause for manifest epilepsy in these patients, whose first fits take place at an age unusual for the onset of genuine epilepsy. A survey of the literature on cases of pure alcohol epilepsy revealed an average age of 28 years for the first convulsion, with no seizures after the cessation of alcoholic abuse. This appears to answer negatively the question whether chronic alcohol intoxication can produce epilepsy which continues after complete abstinence. Bratz,[16] who gave special attention to this problem, never saw an instance of the transition of pure alcohol epilepsy into epilepsy with manifestations in alcohol-free periods.

It appears that alcohol seizures are due not to the alcohol itself but to sudden abstinence after chronic abuse. This becomes understandable when one remembers that alcohol in large doses has a narcotic, and therefore an anticonvulsive action, a fact which has been frequently

13. Féré, E.: L'epilepsie, Paris, Gauthier-Villars et fils, 1896, p. 277.

14. Müller, E. H.: Einige Beziehungen des Alkoholismus zur Aetiologie der Epilepsie, Monatschr. f. Psychiat. u. Neurol. **28**:1, 1910.

15. Cobb, S.; Christian, H. A., and Lennox, W.: Alcohol Poisoning, in Christian, H. A.: Oxford Medicine, New York, Oxford University Press, 1939, vol. 11, p. 909.

16. Bratz, D.: Alkohol und Epilepsie, Allg. Ztschr. f. Psychiat. **56**:334, 1899.

overlooked. Wilson,[17] however, as recently as 1940 stated: "Alcohol has within my knowledge proved a valuable means of warding off a fit in more than one case of those epileptics who feel a fit approaching hours before." The anticonvulsive action of drugs closely related to alcohol, especially paraldehyde and chloral hydrate, is used therapeutically in the management of status epilepticus, both drugs being mentioned here as causes of withdrawal seizures after addiction. Pharmacologic, as well as clinical, considerations, therefore, lead to the conclusion that alcoholic seizures are caused by the same mechanism as the seizures after withdrawal from barbiturates, paraldehyde and other hypnotics of the aliphatic group. This is illustrated by a patient of Schrijver[18] who had seizures after prolonged sleep treatment with barbiturates; the same patient had a history of a few seizures after excessive use of alcohol, occurring for the first time at the age of 25.

The parallelism between seizures and delirium in cases of barbiturate intoxication after sudden withdrawal of the drug is obvious from the literature. Therefore, the question arises whether the same parallelism exists between epileptic seizures and the delirium of alcoholism. The evidence of the facts brought forward in this paper is in favor of the much debated withdrawal theory of the causation of delirium tremens. Kraepelin showed the similarity of barbiturate psychosis and delirium tremens, and the delirium after withdrawal of paraldehyde is like alcoholic delirium up to the physical manifestations, such as sweating. The duration is the same, and only the interval between withdrawal and appearance of the psychosis is longer and, therefore, anamnestically more easily recognizable in paraldehyde delirium than in delirium tremens. Furthermore, the frequency of convulsions before and during delirium tremens is known. There is much evidence against withdrawal as the only explanation of delirium tremens. However, the material collected by Bonhöffer[19] and others cannot be discarded, and withdrawal may be at least one of many factors which lead to delirium, as it obviously did in case 3 in this report. The discussion of abstinence as a cause of alcoholic delirium is confused by the practical question whether or not sudden withdrawal of alcohol is the best therapy for delirium tremens. It is the treatment of choice in the opinion of all competent workers in the field. This opinion, however, is not contrary to the withdrawal theory when one considers that the use of sedatives, such as barbiturates (Sheps[20]) and paraldehyde, as recommended in

17. Wilson, S. A. Kinnier: Neurology, edited by A. N. Bruce, London, Edward Arnold & Co., 1940, p. 1540.

18. Schrijver, D.: Heilung eines Falles von Dementia paranoides nach Dauernarkose, Allg. Ztschr. f. Psychiat. **94**:173, 1931.

19. Bonhöffer, K.: Ueber Alkohol-, Alkaloid- und andere Vergiftungspsychosen, Ztschr. f. ärztl. Fortbild. **8**:415, 1911.

20. Sheps, J. G.: The Role of Abstinence in the Etiology of Delirium Tremens, J. Nerv. & Ment. Dis. **95**:278, 1942.

cases of delirium tremens by Bowman and associates,[21] substitutes the narcotic effects of such drugs for those of the alcohol.

It is probable that epileptic seizures, as well as psychosis, following withdrawal of barbiturates and other drugs are caused by the same mechanism. In my cases of barbital intoxication delirium-like pictures have not been noted, perhaps because the patients were already chronically disturbed. Although convulsions of this type can occur without psychosis, the combination is frequent. Pohlisch,[23b] in a survey of 30 cases of withdrawal psychosis, found that convulsions occurred in 11. The same author[22] found epileptic seizures in 44 of 62 cases of alcoholic delirium. Although some authors[23] have given lower figures, the frequency of convulsions in nonalcoholic withdrawal psychosis and their frequency in delirium tremens are similar. The parallelism between seizures and psychosis after withdrawal of certain drugs is even shown by the negative experience that with the sulfur-containing group of hypnotics and with morphine addiction withdrawal symptoms do not occur; i. e., neither convulsions nor psychotic syndromes have been reported. As to the time relationship between convulsions and the psychosis, it can be said that the seizures frequently precede, but also occur during and even at the end of, the psychosis. Thus, it is obvious that the convulsions do not cause the psychosis, but that both, apparently, are produced by a common mechanism.

Brief mention should be made of ether convulsions. I do not feel that they belong to the same group as the convulsions already described. They are extremely rare and generally occur in young patients with severe toxic-infectious conditions. They end fatally in almost 50 per cent and set in at a time when the patient is still under the anesthetic; therefore the mechanism of withdrawal cannot be accepted. They are almost invariably associated with a rapid rise of temperature to 105, and even to 108, F. and usually occur on very hot days. Many authors have called the conditions heat stroke; others have suggested that impurities of the ether act as a convulsant.[24] Furthermore, the withdrawal seizures described here occur invariably in chronically intoxicated persons; ether anesthesia is an acute intoxication. There is only 1 report on chronic ether addiction, that by Hart,[25] who described ether

21. Bowman, K. M.; Wortis, H., and Keiser, S.: The Treatment of Delirium Tremens, J. A. M. A. **112**:1217 (April 1) 1939.

22. Pohlisch, K.: Die pathogenetische Bedeutung der Gelegenheitsursachen für das Delirium tremens, Monatschr. f. Psychiat. u. Neurol. **63**:69, 1927.

23. Rosenbaum, M.; Lewis, M.; Piker, P., and Goldman, D.: Convulsive Seizures in Delirium Tremens, Arch. Neurol. & Psychiat. **45**:486 (March) 1941.

24. Lundy, J. S., and Touhy, E. B.: General Anesthesia Complicated by Convulsions, J. A. M. A. **108**:971 (March 20) 1937.

25. Hart, E.: An Address on Ether-Drinking: Its Prevalence and Results, Brit. M. J. **2**:885, 1890.

drinking in Ireland but did not mention epileptic seizures. Apparently, the convulsions do not occur with those aliphatic hypnotics which are very volatile and for this reason are used as inhalation anesthetics.

In an attempt to understand the mechanism involved in withdrawal seizures, several possibilities had to be taken into consideration. The clearing up of stupefaction is obviously not an explanation. There is no record of convulsions after sudden withdrawal of the drug in cases of pure morphine addiction. Since opium and its derivatives have a poor anticonvulsive effect,[26] it might appear that only withdrawal of definitely anticonvulsive drugs produces seizures. However, it has been pointed out by Pohlisch [3b] that withdrawal of bromides, even after long use, never leads to psychoses or to epileptic seizures. Psychotic episodes in chronic bromide intoxication occur only during the use of bromides and disappear after withdrawal. Their symptoms are not comparable to the delirium after use of barbiturates, and convulsions do not occur. This is in accordance with the experience that in epileptic persons under treatment with bromides withdrawal of the drug does not so readily lead to status epilepticus as does withdrawal of phenobarbital. Neither does it seem to occur so easily after withdrawal of dilantin medication, although no systematic study of the effect of sudden cessation of this drug is yet available.

It is also possible to explain withdrawal seizures as due to sudden variation of the convulsive threshold. Bromides and soluble barbital were administered to patients under electric shock therapy, and the resulting threshold effects were measured, as will be reported more fully elsewhere. It was found that bromides produce hardly any variation of threshold, whereas soluble barbital causes a definite rise during administration, followed by a fall after withdrawal. This fall of threshold could account for withdrawal seizures after soluble barbital, but not after bromide, intoxication.

There is some evidence that the curve of excretion of the different anticonvulsants may give a hint as to the time when seizures can be expected. From the available studies on excretion of barbitals, it was found that soluble barbital was excreted to 32.8 per cent on the third day, to 10.4 per cent on the fourth day and to 6.8 per cent on the fifth day.[27] No traces of the drug could be found after the eighth day. Most of the soluble barbital had left the body on the fourth or fifth day. A more protracted excretion was found for phenobarbital and barbital.[28] The excretion time of paraldehyde is shorter than that of

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26. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C. Thomas, Publisher, 1941, p. 495.

27. Reinert, M.: Ueber die Ausscheidung von Barbitursäurederivaten im Harn beim Hund, Arch. f. exper. Path. u. Pharmakol. **130**:49, 1928.

28. Reiche, F.: Zur Kenntnis der Veronalvergiftungen und der Veronalausscheidung, Klin. Wchnschr. **5**:2112, 1926.

the barbiturates, and in a still shorter time alcohol leaves the organism. It has been seen that in my material on soluble barbital intoxication seizures occurred after four days. Convulsions after withdrawal of barbital were reported after five to nine days, which is explainable by the aforementioned differences in the excretion of the pure barbital and its sodium salt. The longest interval was reported in a case of addiction to phenobarbital with fits between the ninth and the eleventh day after withdrawal.[3b] Shorter intervals were noted after paraldehyde addiction, in 8 cases of which reported in the literature convulsions occurred on the second or third day after withdrawal. A still shorter interval was seen with alcoholic convulsions. Exactly the same intervals hold good for the psychotic episodes after withdrawal of barbiturates, paraldehyde and, possibly, alcohol. Therefore, some parallelism between the occurrence of convulsions and psychosis and the retention of the respective drug in the body seems to exist.

I do not wish to speculate on the possible role of factors, such as cerebral edema or nutritional deficiency, frequent in all types of addiction. No definite conclusions as to the mechanism involved are possible at present. Drug addiction alone is not a sufficient explanation, for several reasons: 1. Acute intoxication, even with the largest dose of the drugs under discussion, is never followed by convulsions. 2. All the drugs are anticonvulsants. 3. The convulsions occur at a time when most of the drug has been excreted from the body. As to the withdrawal psychosis, it can be added that its symptomatology is completely different from the mental picture of chronic intoxication with the same drugs without withdrawal. Therefore, another process is to be suspected. Kraepelin, cited by Pohlisch,[3b] expressed the belief that certain "metatoxic" products are responsible for this type of seizure, as well as for the psychosis; other authors spoke of a "mediate toxic action." Although this concept is merely a hypothesis, a rather complicated chemical process has to be suspected, inasmuch as, in addition to the withdrawal mechanism, previous chronic intoxication with the respective drug is an absolute condition for the occurrence of both the withdrawal seizures and the psychosis. The chemical changes lead to seizures supposedly only in persons with a specific tendency to convulsions. The probability that the convulsions and the phychosis are determined by a similar mechanism appears as an interesting clinical deduction, at a time when electroencephalography points to new links between epilepsy and the various psychoses.

SUMMARY

The cases of 7 nonepileptic patients who had convulsions four days after withdrawal of soluble barbital are reported; they had been

accustomed to this sedative for one to two years. None of them had seizures prior to or after this occurrence.

Seizures occur after withdrawal of the various barbiturates, paraldehyde and other hypnotics of the aliphatic group. They are seen only after prolonged medication, never after acute intoxication with the same drugs.

The dangerous increase of seizures in epileptic persons following sudden discontinuance of phenobarbital is explainable by the same mechanism. It seems that in this respect phenobarbital acts differently from other anticonvulsive drugs, such as bromides and dilantin.

The literature on withdrawal seizures after chronic intoxication with such hypnotics as barbiturates and paraldehyde reveals that these convulsions, in most instances, are associated with a delirium-like psychosis of several days' duration.

Withdrawal seems to be equally responsible for convulsions in cases of so-called alcohol epilepsy. Alcohol in large doses is a narcotic, and fits occur only during the sobering-up process, as demonstrated in 2 cases reported here. The possible relation between alcoholic delirium and seizures and the analogous manifestations in intoxication with barbiturates and paraldehyde are discussed.

Ether convulsions are mentioned as not belonging in the group of withdrawal seizures.

The time interval between withdrawal and convulsions or psychosis is rather constant for each drug.

No immediate action of the drug, but some unknown physicochemical process developing after withdrawal in a chronically intoxicated patient, seems to be responsible for both the convulsions and the withdrawal psychosis.

Drs. P. V. Brikates, H. Brill and R. F. Binzley, Pilgrim State Hospital, brought the various cases to my attention.

Pilgrim State Hospital.

ELECTROENCEPHALOGRAM ACCOMPANYING HYPERACTIVE CAROTID SINUS REFLEX AND ORTHOSTATIC SYNCOPE

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Since studies on the electrical activity of the cortex have shown that in sleep,[1] in epileptic seizures [2] and in cerebral anoxia [3] characteristic changes occur, it seemed possible that similar studies might help in distinguishing between the syncope occurring with different types of hyperactive carotid sinus reflex and might lead to a better understanding of the mechanisms responsible for loss of consciousness.

The three types of carotid sinus syncope distinguished by Weiss and Baker [4] are the cardiodepressor, in which pressure on the carotid sinus causes slowing of the heart rate and a subsequent critical fall in systemic blood pressure; the vasodilator, in which a critical fall in blood pressure occurs without a significant decrease in heart rate, and the central, in which consciousness is lost without a significant fall in blood pressure. Weiss and Baker pointed out, however, that these pure types are the exception rather than the rule and that in any given case careful study is necessary before one can say definitely whether unconsciousness is caused by a decrease in heart rate, a vasodilatation or a central reflex.

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1. Loomis, A. L.; Harvey, E. N., and Hobart, G.: Electrical Potentials of the Human Brain, J. Exper. Psychol. **19**:249-279, 1936.

2. (*a*) Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electro-Encephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133-1148 (Dec.) 1935. (*b*) Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Epilepsy: A Paroxysmal Cerebral Dysrhythmia, Brain **60**:377-388, 1937.

3. (*a*) Sugar, O., and Gerard, R. W.: Anoxia and Brain Potentials, J. Neurophysiol. **1**:558-572, 1938. (*b*) Gibbs, Davis and Lennox.[2a]

4. Weiss, S., and Baker, J. P.: Carotid Sinus Reflex in Health and Disease: Its Rôle in Causation of Fainting and Convulsions, Medicine **12**:297-354, 1933.

For the purposes of the present study, the cardiodepressor and the vasodilator type are grouped together and called the circulatory.

Lennox, Gibbs and Gibbs [5] found that if the blood pressure falls or the oxygen in the respired air is reduced, consciousness is lost when, and only when, blood returning from the brain becomes less than 30 per cent saturated with oxygen. Studies by Lennox, Gibbs and Gibbs [5] and by Ferris, Capps and Weiss [6] showed that in some cases of carotid sinus syncope of the circulatory type (i. e., in cases in which there is a great fall in blood pressure) there is a sufficient decrease in the oxygen tension of blood passing through the brain to account for the loss of consciousness. In cases of the central type of carotid sinus syncope, however, Lennox, Gibbs and Gibbs [5] and Ferris, Capps and Weiss [6] obtained samples of internal jugular venous blood during syncope which had a normal oxygen saturation (60 to 67 per cent). Because of the high level of cerebral oxygen tension indicated by these samples, both groups of investigators concluded that some factor other than generalized cerebral anoxia must produce unconsciousness in the central type of carotid sinus syncope.

Four previous studies have dealt with electroencephalographic changes associated with carotid sinus syncope. Lennox, Gibbs and Gibbs [7] reported high voltage slow waves followed by flattening of the record in cases of carotid sinus syncope of the cardiac type. Margolin, Strauss and Engel,[8] in a preliminary report, referred to the occurrence of 4 per second waves in carotid sinus syncope, and Engel and Margolin,[9] in a longer report, spoke of slow waves as a prominent feature of the electroencephalogram during carotid sinus syncope. The only study which has focused on the problem of carotid sinus syncope of the central type is that by Romano, Stead and Taylor.[10] These authors reported

5. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Relationship of Unconsciousness to Cerebral Blood Flow and to Anoxemia, Arch. Neurol. & Psychiat. **34**:1001-1013 (Nov.) 1935.

6. Ferris, E. B., Jr.; Capps, R. B., and Weiss, S.: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions, Medicine **14**:377-456, 1935.

7. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: The Relationship in Man of Cerebral Activity to Blood Flow and to Blood Constituents, J. Neurol. & Psychiat. **1**:211-225, 1938.

8. Margolin, S. G.; Strauss, H., and Engel, G. L.: Electroencephalographic Changes Associated with Hypersensitivity of the Carotid Sinus, Arch. Neurol. & Psychiat. **45**:889-890 (May) 1941.

9. Engel, G. L., and Margolin, S. G.: Neuropsychiatric Disturbances in Internal Disease: Metabolic Factors and Electroencephalographic Correlations, Arch. Int. Med. **70**:236-259 (Aug.) 1942.

10. Romano, J.; Stead, E. A., Jr., and Taylor, Z. E.: Clinical and Electroencephalographic Changes Produced by a Sensitive Carotid Sinus of the Cerebral Type, New England J. Med. **223**:708-712, 1940.

1 case in which no slow waves appeared during syncope, but only fast activity. The electroencephalograms in this case were taken and interpreted in our laboratory.[11]

In a preliminary study, the electroencephalogram was found to show no definite evidence of slowing in carotid sinus syncope of either type and to be similar in both types. It was decided that a parallel study would have to be conducted on orthostatic syncope, for knowledge of the electroencephalographic changes occurring in that condition was based on a single observation of a subject with epilepsy.[2a] Pertinent data might have been obtained from animal experiments in which the blood pressure was decreased[12] or the cerebral arteries were ligated[13] or from the study of Yeager and Walsh,[14] in which the carotid arteries of a man were ligated. It was deemed unwise, however, to accept such studies as presenting situations entirely analogous to the acute hypotension encountered in cases of carotid sinus syncope. For this reason, observations were included on 3 healthy young men during a sudden critical fall in blood pressure.

MATERIAL AND METHOD

A total of 17 patients with hypersensitive carotid sinus reflexes were studied during a twenty minute control period and also immediately before and during syncope produced by digital pressure on the sensitive carotid sinus. Twelve subjects had the circulatory type (i. e., either cardiodepressor or vasodilator) and 5 the central type. Three normal subjects were given 5½ grains (0.358 Gm.) of sodium nitrite by mouth and placed on a tipping table. In each a critical fall in blood

11. The cortical spectrums showed a series of humps, or broad harmonics, which we have since identified as an artefact due to a splice in the film. This artefact is obtained whenever an exceedingly low voltage record is amplified for purposes of analysis beyond a permissible limit.

12. Adrian, E. D., and Matthews, B. H. C.: The Interpretation of Potential Waves in the Cortex, J. Physiol. **81**:440-471, 1934. Beecher, H. K.; McDonough, F. K., and Forbes, A.: Effects of Blood Pressure Changes on Cortical Potentials During Anesthesia, J. Neurophysiol. **1**:324-331, 1938.

13. (*a*) Bremer, F.: Quelques propriétés de l'activité électrique du cortex cérébral "isolé," Compt. rend. Soc. de biol. **118**:1241-1244, 1935. (*b*) Simpson, H. N., and Derbyshire, A. J.: Electrical Activity of the Motor Cortex During Cerebral Anemia, Am. J. Physiol. **109**:99, 1934. (*c*) Asenjo, A.: Ueber die Wirkung des extrakraniellen Verschlusses der Hirngefässe auf die bioelektrische Tätigkeit der Hirnrinde, Zentralbl. f. Neurochir. **4**:41-46, 1939; (*d*) Lokalisierte bioelektrische Ableitungen von der Hirnrinde bei experimentellen Störungen des Blutkreislaufs des Gehirns. Abklemmung der Carotis communis, ibid. **3**:198-203, 1938. Sugar and Gerard.[3a]

14. Yeager, C. L., and Walsh, M. N.: Changes in the Electro-Encephalogram from Ligation of the Carotid Arteries, in the Case of Intracranial Saccular Aneurysm, J. A. M. A. **114**:1625-1626 (April 27) 1940.

pressure occurred when placed in the vertical, head-up position. Two of these subjects lost consciousness, and the other became confused. This method of causing syncope was suggested to Lennox, Gibbs and Gibbs [5] by Dr. Soma Weiss, who with his co-workers [15] made a detailed study of the associated circulatory changes. The response to compression of the carotid sinus was studied in two control groups, consisting of 15 normal subjects and 20 epileptic patients.

The electrical activity of the frontal, the parietal and the occipital area was recorded with a multichannel Grass electroencephalograph. Unipolar leads were employed, the indifferent electrode being connected to the two ear lobes. In all but 2 of the subjects in whom syncope was produced the electrocardiogram was simultaneously recorded.

In 8 of the 17 patients with a hyperactive carotid sinus reflex and in all the control subjects, the activity of the right occipital area was recorded on film as a shadowgram, and spectrums from strips of this record were obtained by the Grass method of frequency analysis.[16]

In the case of each subject one sinus was compressed at a time, but in all cases both sinuses were studied. The procedure was divided into six steps, as follows: (1) The examiner was seated beside the subject, who sat quietly in a chair with the eyes closed; (2) the examiner's hand was placed on the subject's neck; (3) digital pressure was applied to the carotid sinus; (4) the reaction (if any) was recorded; (5) pressure on the sinus was released, and (6) the hand was removed from the neck.

Records and spectrums obtained during each of these steps were compared. Movement artefacts are a serious source of error in such experiments. All possible care was taken to avoid them. When they appeared in the record, they were usually identifiable by their characteristic appearance or by identical sways and irregular waves in the electrocardiogram.

RESULTS

Carotid Sinus Syncope.—First Series (9 patients, without spectrum analysis, 7 of whom had the circulatory and 2 the central type):

In this series the usual change associated with syncope was a decrease in amplitude with little or no evidence of slowing (table 1; figs. 1, 3 and 4). The few slow waves that appeared were usually interpretable as movement artefacts. One patient with the circulatory type, however, showed a short period of moderately slow activity just as consciousness was lost; during unconsciousness there was, as usual, a great decrease in amplitude (table 1, case 7; fig. 2).

Second Series (8 patients, with spectrum analysis, 5 of whom had the circulatory and 3 the central type): In this series there was no patient in whose record slow waves were a prominent feature during

15. Wilkins, R. W.; Weiss, S., and Haynes, F. W.: The Effect of Epinephrin in Circulatory Collapse Induced by Sodium Nitrite, J. Clin. Investigation **17**:41-51, 1938.

16. Grass, A. M., and Gibbs, F. A.: A Fourier Transform of the Electroencephalogram, J. Neurophysiol. **1**:521-526, 1938.

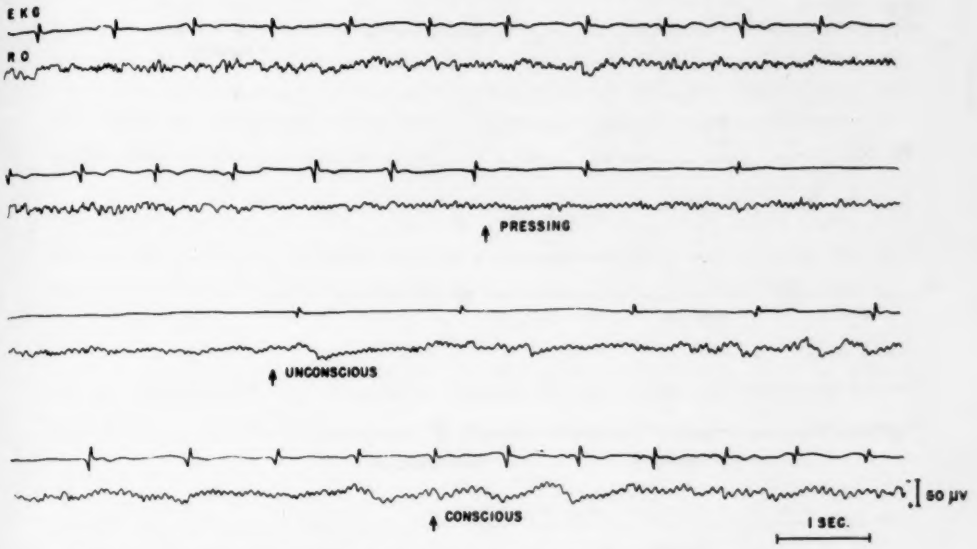

Fig. 1.—Electroencephalogram in a case of cardiopressor type of carotid sinus syncope, showing the usual response, a decrease in amplitude without gross evidence of slowing.

R O, electroencephalogram from the right occipital area, with indifferent electrodes on the lobes of both ears; *E K G*, electrocardiogram. At the point marked pressing the right carotid sinus was compressed. Consciousness was lost and regained at the points indicated. The record is continuous; no time is omitted between strips. Time and voltage calibrations are shown in the lower right corner.

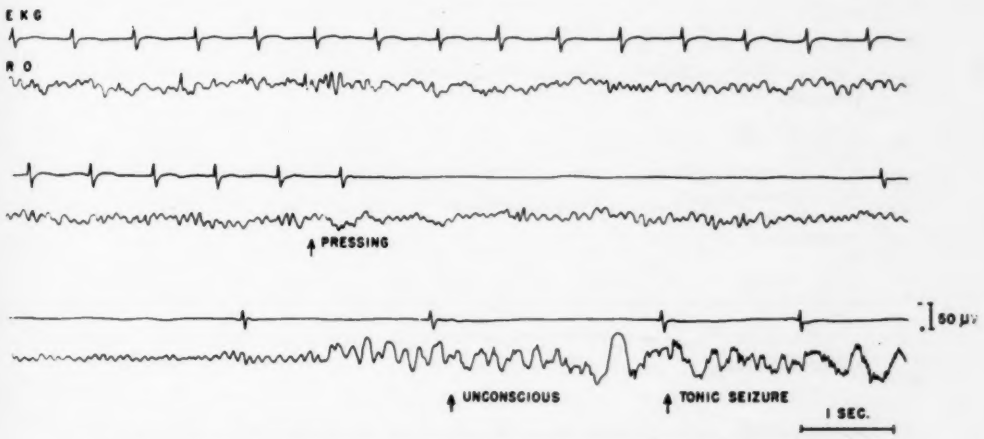

Fig. 2.—Electroencephalogram in a case of cardiopressor type of carotid sinus syncope, showing an unusual response, an increase in amplitude with obvious slowing.

The irregular fast waves that appear after the onset of the tonic seizure are muscle potentials; these increased in voltage and were associated with such large movement artefacts that the record had to be interrupted. The occurrence of a convulsion during carotid sinus syncope is not ordinarily associated with either high voltage fast or slow waves of cortical origin. Labeling as in figure 1. The record is contiuous; no time is omitted between strips.

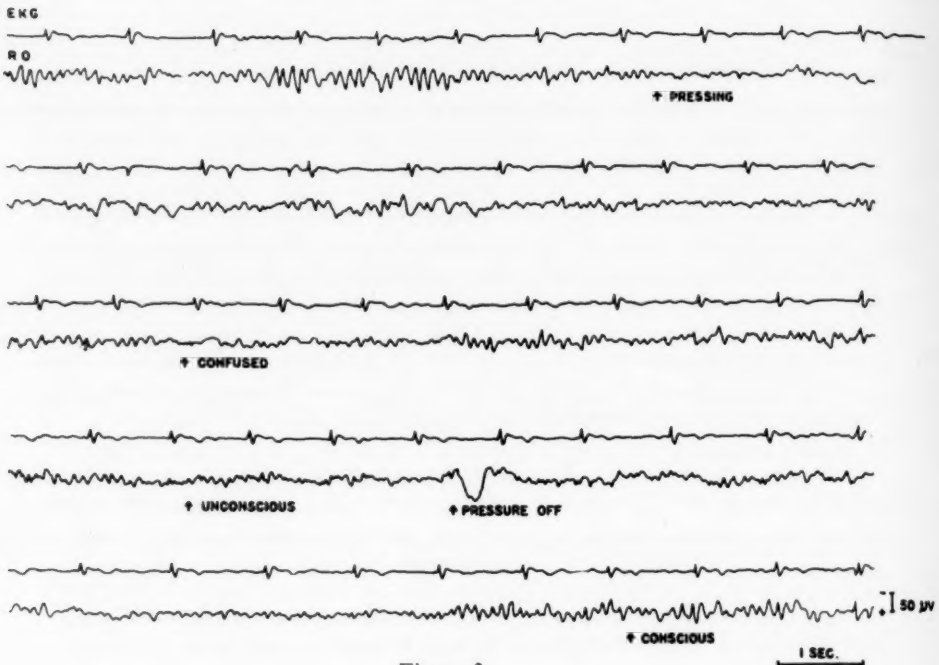

Figure 3

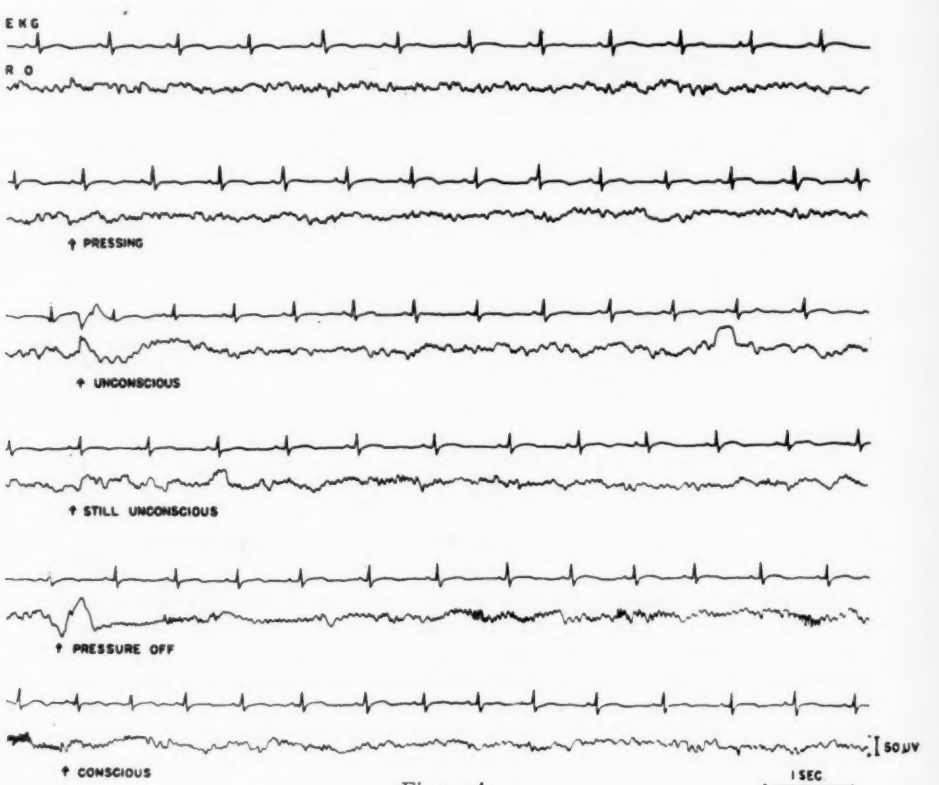

Figure 4

(See legends on opposite page)

syncope (table 2). The records of the 5 patients with the circulatory type, however, showed questionable slowing. All patients, both those with the circulatory and those with the central type, showed a decrease in amplitude during syncope.

By comparing spectrums made from strips of record obtained before and during syncope it was possible to demonstrate that in some cases there was a definite change in frequency. In cases of the circulatory type the frequency tended to shift to the slow side during syncope (fig. 5) and in cases of the central type to the fast side (fig. 6*A*), but

TABLE 1.—*Electroencephalographic Data on Series 1*

Case	Type of Carotid Sinus Syncope	Electroencephalogram		Other Disease Present
		Before	Maximal Change During Reaction *	
1	Circulatory	Abnormal (8-10/sec.)	Flattening; no slowing	Dementia paralytica
2	Circulatory	Normal (9/sec.)	Slow waves (?), followed by flattening	Syphilis
3	Circulatory	Abnormal (4-6/sec.)	Slow waves (?), followed by flattening	None
4	Circulatory	Abnormal (4-6/sec.)	Slow waves (?), followed by flattening	Epilepsy
5	Circulatory	Normal; low voltage fast waves	Flattening; no slowing	General arteriosclerosis
6	Circulatory	Normal; low voltage fast waves	Flattening; no slowing	None
7	Circulatory	Normal; (10/sec.)	Definite slowing, followed by flattening	None
8	Central	Normal; (10/sec.)	Flattening; no slowing	None
9	Central	Normal; low voltage fast waves	Flattening; no slowing	None

* In each case the left and the right carotid sinus were compressed several times. The most extreme change that was obtained is given in the table.

EXPLANATION OF FIGURES 3 AND 4

Fig. 3.—Electroencephalogram in a case of the central type of carotid sinus syncope, showing the usual response, a slight decrease in amplitude with no evidence of slowing but possibly a slight increase in fast activity.

Labeling as in figure 1. The record is continuous; no time is omitted between strips.

Fig. 4.—Electroencephalogram in a case of the central type of carotid sinus syncope, showing the usual response, a slight decrease in amplitude with no definite evidence of slowing.

The irregular slow waves that appear in this record are interpreted as artefacts. The four short runs of fast potentials which look like thickenings of the line following the signal *pressure off* are bursts of muscle potential, probably due to swallowing. Labeling as in figure 1. The record is continuous; no time is omitted between strips.

equivocal shifts in frequency were so common that no clearcut distinction between types can be made on this basis.

Orthostatic Syncope.—All 3 of the normal subjects who were given 5½ grains of sodium nitrite by mouth and, after a twenty minute wait, were tipped into a vertical, head-up position, showed high voltage slow waves as they became confused. The 2 subjects who fainted showed exceedingly slower waves during the period of unconsciousness (fig. 4). Spectrum analysis revealed definite evidence of slowing (fig. 6 *A*).

TABLE 2.—*Electroencephalographic Data on Series 2*

Case	Type of Carotid Sinus Syncope	Electroencephalogram		Spectrum Maximal Shift During Syncope *	Other Disease Present
		Before	Maximal Change During Reaction *		
1	Circulatory	Normal (9/sec.)	Slow waves (?), followed by flattening	— ¾ cycle/sec.	None
2	Circulatory	Abnormal (4-10/sec.)	Slow waves (?), followed by flattening	—1 cycle/sec.	General arteriosclerosis
3	Circulatory	Normal (10/sec.)	Slow waves (?), followed by flattening	+ ½ cycle/sec.	None
4	Circulatory	Abnormal (6-10/sec.)	Flattening; no slow waves	± (?)	General arteriosclerosis
5	Circulatory	Abnormal (11/sec. with diphasic spikes)	Flattening; no slow waves	— ½ cycle/sec.	Dementia paralytica
6	Central	Normal (9½/sec.)	Slow waves (?), followed by flattening	+1 cycle/sec.	None
7	Central	Normal; low voltage fast waves	Flattening; no slow waves	± ?	None
8	Central	Normal; low voltage fast waves	Flattening; no slow waves	+1½ cycles/sec.	None

* In each case the left and the right carotid sinus were compressed several times. The most extreme change that was obtained is given in the table.

Control Groups.—Compression of the carotid sinus produced in the normal subjects only a moderate flattening of the record, such as is seen in attention. This response (fig. 7 *B*) was qualitatively similar to but quantitatively less than that which occurred during carotid sinus syncope. The epileptic patients responded like the normal subjects except in 2 instances, in which carotid sinus pressure was associated with pronounced slowing of cortical activity, but without syncope or clinical evidence of an epileptic seizure.

Because associated cerebral disease was present in a large proportion of the patients with carotid sinus syncope, no special significance is attached to the fact that in 40 per cent of the patients the previously obtained electroencephalogram was abnormal, as contrasted with a large control group in which 15 per cent had abnormal electroencephalograms

COMMENT

The fact that slow waves predominate in the electroencephalogram as consciousness is lost in orthostatic syncope is in accord with previous studies on the effects of cerebral anoxia produced either by ligating the cerebral arteries [17] or by breathing a low oxygen mixture.[18] It is surprising that obvious slowing is so uncommon in cases of the circulatory type of carotid sinus syncope. Previous studies [19] have emphasized such slowing. Lennox, Gibbs and Gibbs,[7] however, mentioned flattening of the record after the appearance of slow waves. They described a case which was exactly comparable to one of ours (table 1, case 7, and fig. 3),

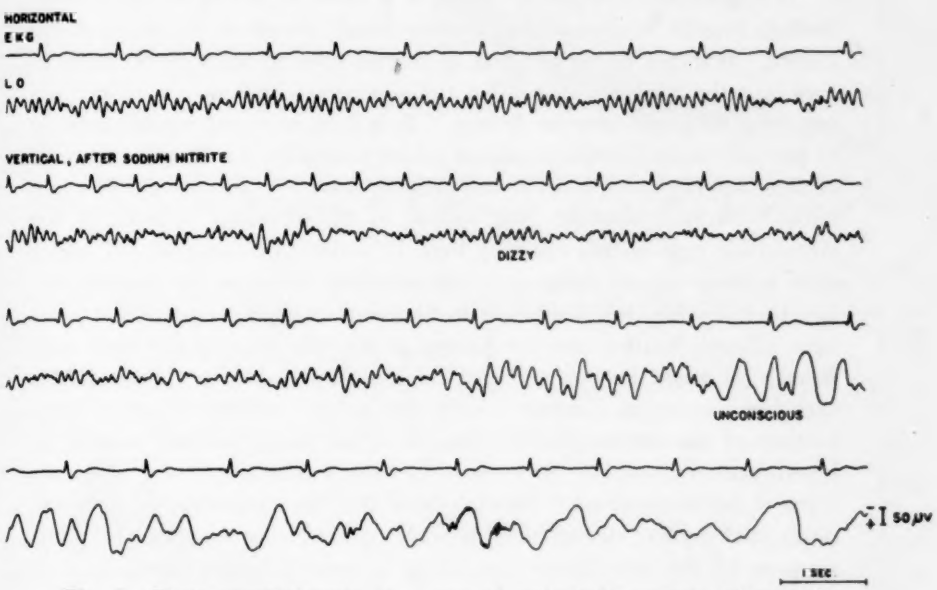

Fig. 5.—Electroencephalogram in a case of orthostatic syncope induced with the aid of sodium nitrite.

The high voltage slow waves that appear with loss of consciousness are usual in this condition. *L O* indicates left occipital lead; *horizontal,* subject recumbent; *vertical,* subject in vertical, head-up position twenty minutes after being given 5½ grains of sodium nitrite by mouth. Other labeling as in figure 1. An interval of twenty minutes occurred between the first two strips; the remainder of the record is continuous.

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17. Sugar and Gerard.[3a] Simpson and Derbyshire.[13b] Yeager and Walsh.[14]

18. Davis, H., and Davis, P. A.: The Electrical Activity of the Brain: Its Relation to Physiological States and to States of Impaired Consciousness, A. Research Nerv. & Ment. Dis., Proc. (1938) **19**:50-80, 1939. Gibbs, Davis and Lennox.[2a] Lennox, Gibbs and Gibbs.[7]

19. Lennox, Gibbs and Gibbs.[7] Margolin, Strauss and Engel.[8] Engel and Margolin.[9]

but such instances are rare; only 1 was seen among the 12 cases of the circulatory type in our series. It seems proper to regard such a case as representing a transition between carotid sinus syncope and orthostatic syncope. Since spectrum analysis revealed evidence of slowing in the majority of cases of carotid sinus syncope of the circulatory type and since slow waves were more common in the unanalyzed records in cases of the circulatory type, it is probable that slowing of cortical activity does tend to occur during carotid sinus syncope of the circulatory type, but it should be remembered that slow waves are by no means a constant and characteristic feature of the record.

It is generally recognized that slow activity is indicative of an intermediate type of injury and that extreme injury results in flattening of the record. It might be argued that in carotid sinus syncope of the circulatory type the anoxia is so sudden and so extreme that slow activity does not have sufficient time to develop. It is easy in experimental animals to produce sudden cerebral anemia which results in the disappearance of cortical activity without evidence of slow waves.[20] Lennox, Gibbs and Gibbs [5] showed, however, that anoxia in carotid sinus syncope of the circulatory type is less extreme than in orthostatic syncope (in which slow activity is very evident). Furthermore, how can one explain the fact that slowing does not occur in the many trials in which blood pressure falls moderately and the patient is not unconscious but only confused? It might be assumed that the slow waves which appear during orthostatic syncope (induced with the aid of sodium nitrite) occur because of low carbon dioxide tension in the brain, and not because of low oxygen tension, but the work of Lennox, Gibbs and Gibbs [5] does not support this assumption. They reported that the carbon dioxide content of internal jugular venous blood is more reduced in cases of carotid sinus syncope of the circulatory type than in cases of orthostatic syncope (induced with the aid of sodium nitrite). It is, of course, possible that sodium nitrite itself is in some way responsible for the slow waves, but how or why it is difficult to imagine. The most reasonable explanation appears to be that in carotid sinus syncope of the circulatory type slow activity is suppressed by a direct cortical accelerator effect of sinus stimulation. This accelerator effect appears in its purest form in syncope of the central type. The acceleration is sufficient, in some cases, to be comparable to that which occurs at the onset of a grand mal epileptic seizure.

We believe that the central type of carotid sinus reflex is a special type of trigger zone epilepsy, with only slight evidence of cortical involvement.

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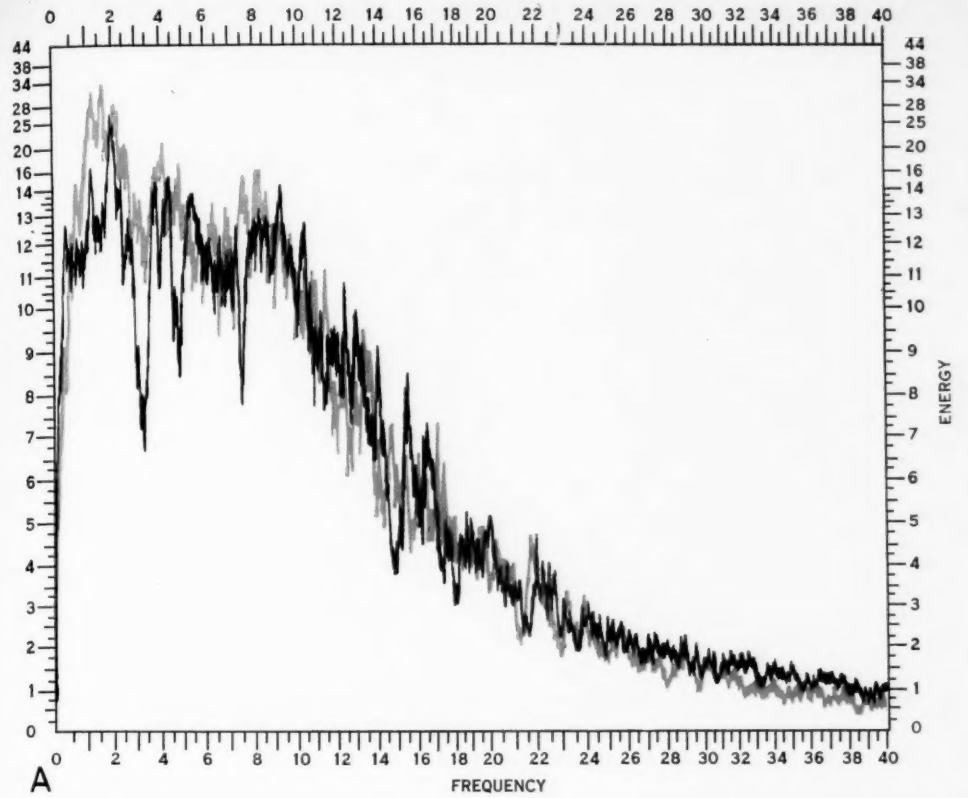
20. Simpson and Derbyshire.[13b] Asenjo.[13c] Asenjo.[13d] Sugar and Gerard.[3a]



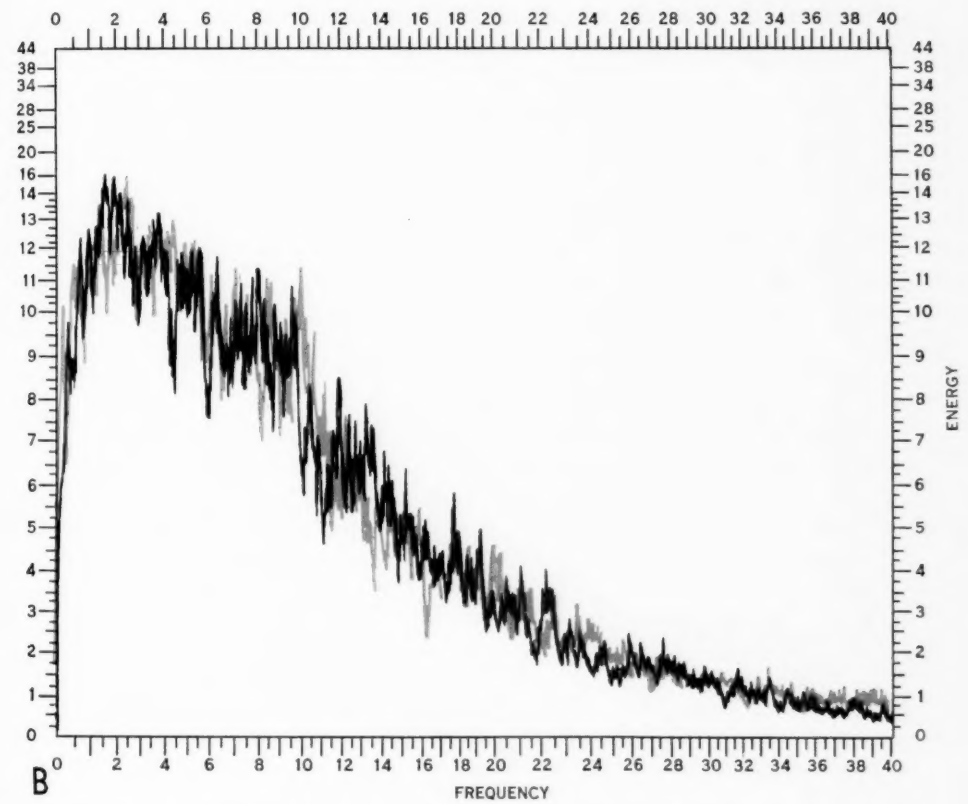


Fig. 6.—*A*, slight shift in energy to the slow side of the cortical spectrum in a case of the cardiopressor type of carotid sinus syncope. These curves were obtained by analyzing the electroencephalogram from the right occipital area. Black curve, before pressing on the sinus; red curve, during syncope. *B*, slight shift in energy to the fast side of the cortical spectrum in a case of the central type of carotid sinus syncope. These curves were obtained by analyzing the electroencephalogram from the right occipital area. Black curve, before pressing on the sinus; red curve, during syncope.

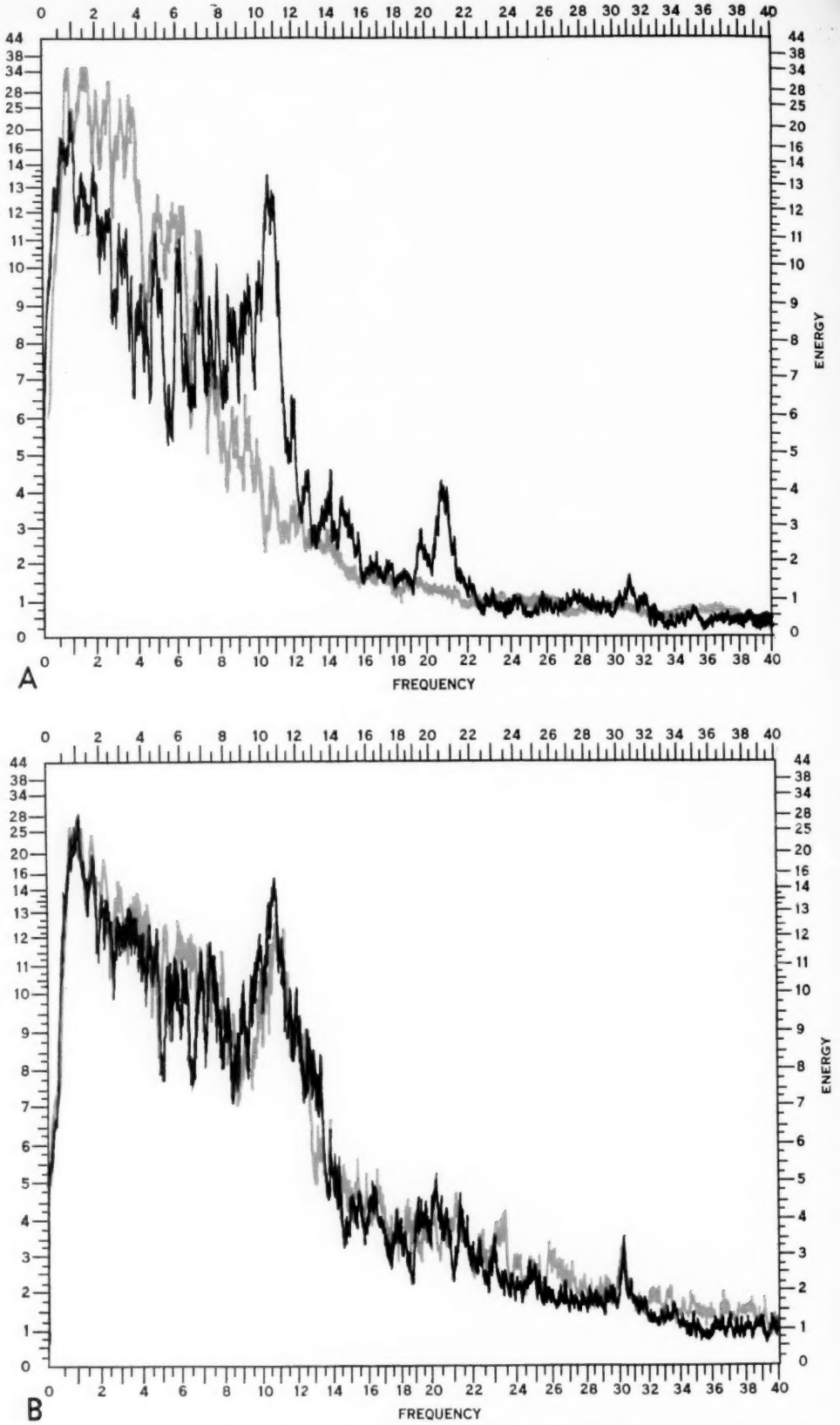


Fig. 7.—*A*, extreme shift in energy to the slow side of the cortical spectrum in a case of orthostatic syncope. These curves were obtained by analyzing the electroencephalogram from the right occipital area. Black curve, before syncope; red curve, during syncope. *B*, slight shift in energy to the fast side of the cortical spectrum with pressure on the carotid sinus in a control subject. This type of response occurs commonly with moderate attention. These curves were obtained by analyzing the electroencephalogram from the right occipital area. Black curve, before pressure on the sinus; red curve, during pressure on the sinus.

CONCLUSIONS

The electrical activity of the cortex has been studied in 17 patients with hyperactive carotid sinus reflexes and in 3 normal subjects in whom orthostatic hypotension developed after the ingestion of sodium nitrite. Electroencephalograms and cortical frequency spectrums were obtained before and during syncope. As a control, the response to compression of the carotid sinus was studied in 15 normal subjects and in 20 epileptic patients.

On the basis of these studies, the following conclusions were drawn.

Slow waves are a prominent feature of the electroencephalogram in orthostatic syncope.

Slow waves of cortical origin are not prominent in carotid sinus syncope of either the circulatory or the central type, and ordinarily no gross disorder of the cortical rhythm is apparent during the syncope.

The most characteristic change that occurs in all types of carotid sinus syncope is a sudden decrease in amplitude; this change is difficult to distinguish from an ordinary attention response.

In rare cases of the cardiodepressor type a short period of slow activity occurs just before consciousness is lost.

In the majority of cases of carotid sinus syncope of the circulatory type spectrum analysis with the Grass analyzer reveals slowing of cortical activity during the period of unconsciousness.

In the majority of cases of carotid sinus syncope of the central type spectrum analysis reveals an increase in the frequency of cortical activity during the period of unconsciousness.

The failure to find evidence of gross slowing of cortical activity in cases of the circulatory type of carotid sinus syncope is explained by the assumption that cortical activity is primarily accelerated by stimulation of the carotid sinus and that it is stopped, rather than slowed, by the sudden cerebral anemia.

The central type of hyperactive carotid sinus reflex can be considered a type of trigger zone epilepsy in which there is only slight cortical involvement.

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EFFECT OF HYPERVENTILATION ON ELECTRO-ENCEPHALOGRAM OF SCHIZOPHRENIC AND NONPSYCHOTIC SUBJECTS

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The present study constitutes an investigation of the comparative reactivity of the central nervous systems of normal and of schizophrenic subjects to metabolic stress (hyperventilation) as indicated by changes in the electroencephalogram.

Although schizophrenic patients as a group exhibit more variability in the amount of alpha activity in their day to day electroencephalograms than do nonpsychotic persons,[1] there are no qualitative distinguishing characteristics. Abnormalities in the electroencephalograms in schizophrenic persons have been reported,[2] but in my experience the incidence of abnormalities is no greater than in the electroencephalograms of an unselected, nonpsychotic population. The possibility exists, however, that there are characteristic differences which are commonly submerged, but which could be brought out under special test conditions.

It is common knowledge that large, slow waves appear in the normal electroencephalogram during hyperventilation. This constitutes an all or none, readily recognizable, objective criterion as to the effect of stress induced by overbreathing. Overventilation as a variable is pertinent to a study of schizophrenia, since it is primarily a metabolic stress (increasing alkalinity of the blood, decreasing carbon dioxide tension, causing vasoconstriction in the brain, etc.). It has previously been shown that altered metabolism is a characteristic of schizophrenia[3]

From the Memorial Foundation for Neuro-Endocrine Research, Worcester State Hospital.

1. Rubin, M. A.: A Variability Study of the Normal and Schizophrenic Occipital Alpha Rhythm, J. Psychol. **6**:325, 1938.

2. Davis, P. A.: Evaluation of the Electroencephalogram of Schizophrenic Patients, Am. J. Psychiat. **96**:851, 1940. Davis, P. A., and Davis, H.: The Electroencephalogram of Psychotic Patients, ibid. **95**:1007, 1939. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: The Likeness of the Cortical Dysrhythmias of Schizophrenia and Psychomotor Epilepsy, ibid. **95**:255, 1938. Jasper, H. H.; Fitzpatrick, C. P., and Solomon, P.: Analogies and Opposites in Schizophrenia and Epilepsy; Electroencephalographic and Clinical Studies, ibid. **95**:835, 1939.

3. Hoskins, R. G.: Oxygen Metabolism in Schizophrenia, Arch. Neurol. & Psychiat. **38**:1261 (Dec.) 1937. Rheingold, J. C.: Autonomic Integration in Schizophrenia: Autonomic Status Determined Statistically, the Thyroid Factor, and a Possible Thyroid-Hypothalamus Mechanism, Psychosom. Med. **1**:397, 1939.

and that schizophrenic persons are best differentiated from nonpsychotic persons when placed under stress.[4] Furthermore, the electroencephalogram has been shown in numerous studies, at Worcester and elsewhere (Hoagland[5]; Rubin, Cohen and Hoagland,[6] and others), to follow alterations in brain metabolism. These considerations led to the choice of hyperventilation as the most promising means of uncovering differences which might exist between the electroencephalograms of schizophrenic and normal subjects.

METHOD

Thirty-five physically healthy, male schizophrenic patients, varying in age from 21 to 47 years (mean age, 31.8 ± 7.0 years), were studied. Thirty per cent of the patients had been hospitalized less than one year, 20 per cent from one to four years, 25 per cent from four to ten years and 25 per cent from ten to twenty-two and a half years. The subtypes of schizophrenias were represented as follows: hebephrenic, 40 per cent; paranoid, 30 per cent; catatonic, 10 per cent; simple and mixed, 20 per cent. The patients were selected at random, except that only those who were cooperative in the test procedure could be used.

Thirty-five nonpsychotic persons were employed as normal control subjects. They ranged in age from 17 to 51 years (mean, 26.0 ± 6.4 years). This group was made up of 21 hospital attendants, 10 college students and 4 members of the professional staff of the hospital.

The subjects reclined, with eyes closed, on a bed in a shielded, semidark room. Electroencephalograms were recorded simultaneously from 3 mm. lead-solder electrodes placed on the occiput, vertex and forehead on the right side. A pair of leads on the mastoid processes served as the reference electrodes. Grass amplifiers and ink-writing oscillographs were employed. After a preliminary base line tracing was obtained, the subject was asked to hyperventilate at a rate of 30 inhalations per minute for two minutes, with emphasis on the expirations. The electroencephalogram was recorded during the overventilation and for three to five minutes after it. After a rest period of five to ten minutes the procedure was repeated.

Observations on both the schizophrenic and the control subjects were evenly distributed throughout the day (from 9 a. m. to 4 p. m.), so that the time of day might be eliminated as a systematic variable in the investigation.

RESULTS

Alpha Activity.—The first hyperventilation uncovered no striking differences between patients and normal control subjects so far as their per cent time alpha was concerned. The amount of alpha activity of some members of each group increased on overventilation. As may

4. Angyal, A., and Blackman, N.: Paradoxical Vestibular Reactions in Schizophrenia Under the Influence of Alcohol, of Hyperpnea and CO_2 Inhalation, Am. J. Psychiat. **97**:894, 1941.

5. Hoagland, H.: Pacemakers of Human Brain Waves in Normals and in General Paretics, Am. J. Physiol. **116**:604, 1936.

6. Rubin, M. A.; Cohen, L. H., and Hoagland, H.: The Effect of Artificially Raised Metabolic Rate on the Electroencephalogram of Schizophrenic Patients, Endocrinology **21**:536, 1937.

be seen in the table, the majority of subjects in each group showed a decrease in per cent time alpha. The number of subjects with an increase in the per cent time alpha in the region of the forehead was about the same as the number with a decrease in the same area. Almost no subject's per cent time alpha remained unchanged.

As compared with the influence of the first hyperventilation, a second hyperventilation within five to ten minutes after the first was less effective in altering the per cent time alpha. Approximately one quarter of the subjects in each group showed no change in per cent time alpha in any region of the head (table). There also was a sharp reduction, as compared with the first hyperventilation, in the percentage of schizophrenic patients whose occipital per cent time alpha decreased (a change from 77 to 37 per cent). This constituted the only clear difference in the two groups as a consequence of the second hyperventilation.

Effects of Two Successive Periods of Hyperventilation on the Per Cent Time Alpha in the Occiput, Vertex and Forehead of Normal Control and of Schizophrenic Subjects

		Percentage of Subjects					
		Normal			Schizophrenic		
	Hyperventilation	Occiput	Vertex	Forehead	Occiput	Vertex	Forehead
Decrease	First	81	81	56	77	63	54
	Second	70	44	56	37	43	31
Increase	First	13	19	44	23	37	46
	Second	13	31	17	37	31	40
No change	First	6	0	0	0	0	0
	Second	17	25	27	26	26	29

It might be mentioned here that alterations in per cent time alpha did not necessarily take place in all regions of the head. It was not uncommon to find a noticeable decrease in the occiput with no accompanying change in the other regions. In some instances an increase in one region occurred simultaneously with a decrease in other areas, further indicating the relative independence of alpha activity in the various regions of the brain.[7]

Alterations in per cent time alpha were found to occur immediately at the beginning of hyperventilation or at any time thereafter. They were usually over within a minute or so and were not correlated with the commonly occurring apnea or paresthesia (tingling or numbness in the face and extremities, muscle twitching, dizziness, etc.).

Figures 1 and 2 are illustrative of the magnitude of the increases and decreases in per cent time alpha resulting from hyperventilation.

7. Rubin, M. A.: The Distribution of the Alpha Rhythm over the Cerebral Cortex of Normal Man, J. Neurophysiol. **1**:313, 1938.

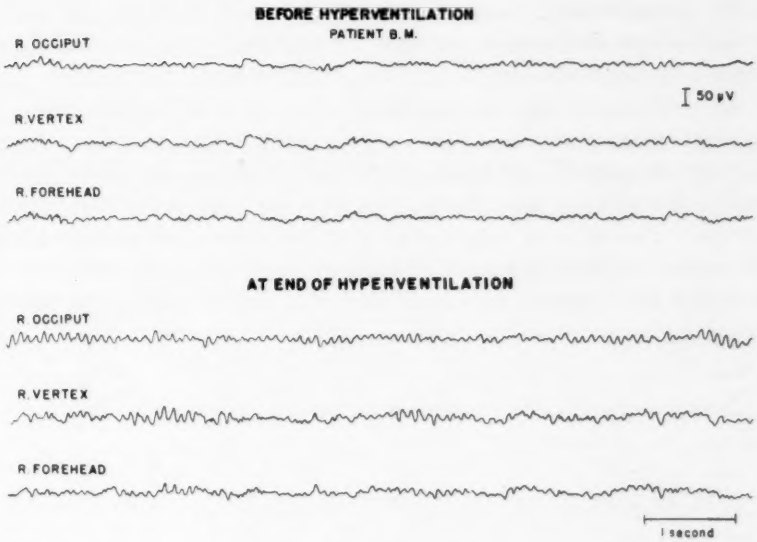

Fig. 1.—Simultaneous records from the occiput, vertex and forehead on the right side, illustrating an increase in per cent time alpha occurring toward the end of a two minute period of hyperventilation. Amplification constant throughout.

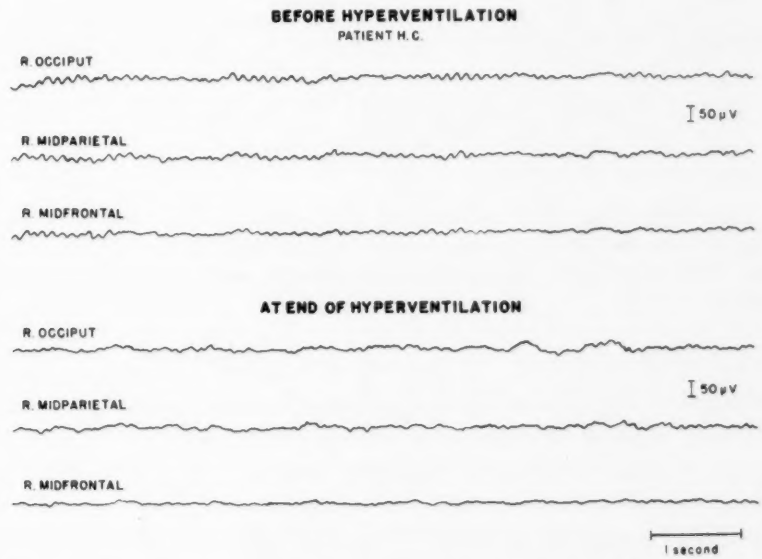

Fig. 2.—Simultaneous records from the occiput, vertex and forehead on the right side, showing a decrease in per cent time alpha near the end of a two minute period of hyperventilation. Amplification constant throughout.

The tracings were taken from 2 schizophrenic patients, but are typical of the corresponding changes in normal control subjects. It may be noted that an increase in per cent time alpha is accompanied by an increase in amplitude, and a decrease, by a decrease in amplitude.

Slow Waves.—The most striking effect of hyperventilation on the electroencephalogram was the appearance of large, slow fluctuations of potential. They usually appeared about one and a half minutes after overbreathing was started, their onset frequently being rather sudden. The slowing might consist of a decrease of merely 1 or 2 cycles from the prehyperventilation alpha frequency, or it might decrease to as low as 2 cycles per second (fig. 3). In all cases there was an accompanying increase in amplitude, which was in many cases as great

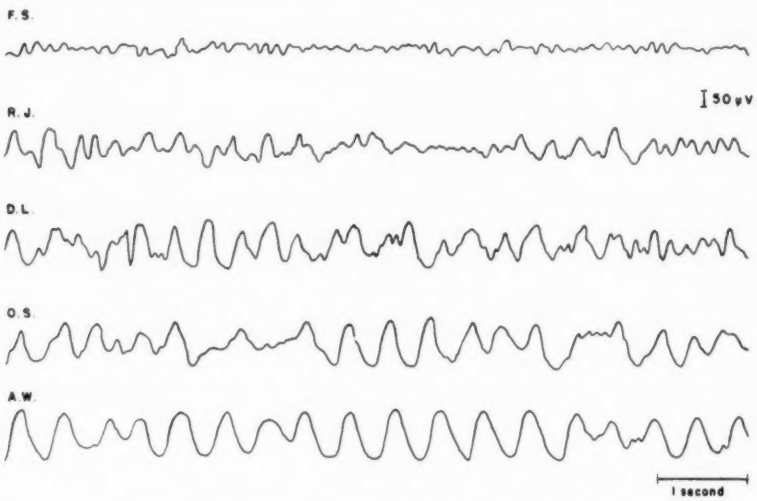

Fig. 3.—Tracings from the forehead of 5 subjects, illustrating the common types of slow wave patterns which appear on hyperventilation. All records were taken immediately after cessation of hyperventilation. Amplification constant throughout.

as 700 to 800 per cent. Sometimes slow activity did not occur until the moment when the two minute period of hyperventilation was ended, and even in those subjects who showed slow waves sooner there was always a further increase in regularity and amount of low frequency activity immediately on cessation of overbreathing. As a general rule, the normal frequency of the electroencephalogram was restored within thirty seconds after the hyperventilation was over. However, in some cases, random, short bursts of slow activity occurred for a minute or two after overventilation ended.

Figure 4 illustrates the differences in slow activity in the electroencephalograms from the occiput and from the forehead after hyperventilation. The occipital region seldom shows the regularity and amplitude of slow waves that the forehead does. The slow rhythms occur first in the region of the forehead and then spread posteriorly over the head. The occiput is the first region to return to its normal frequency, while the forehead is the last (fig. 4). This closely parallels the order of return of the various areas from slow activity to normal frequencies during anesthesia.[8]

The influence of a second hyperventilation within ten minutes after the first was variable. In some instances the period of slow activity

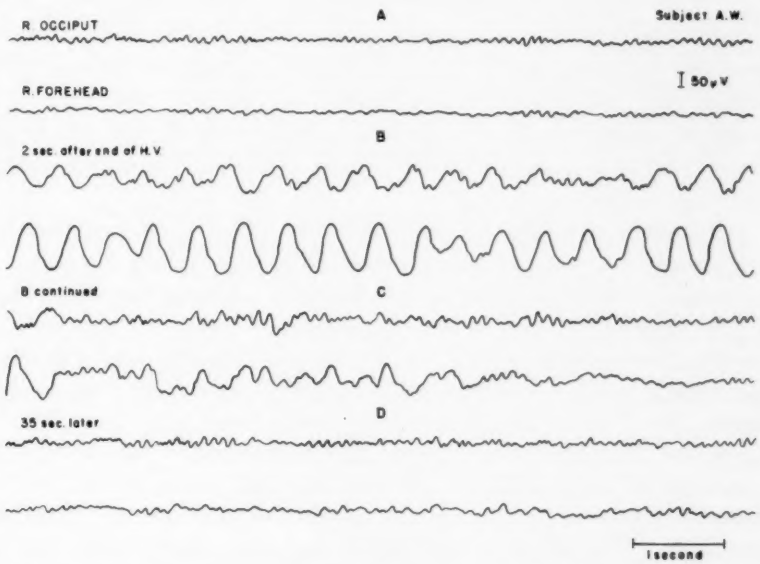

Fig. 4.—Simultaneous records from the occiput and forehead on the right side, illustrating greater synchrony and amplitude of the slow rhythms in the forehead and the earlier return to normal frequency of the occiput. *A*, before hyperventilation; *B*, two seconds after hyperventilation ended; *C*, record continued, and *D*, thirty-five seconds later. Note that in *B* the slow waves in the forehead record are completely out of phase with those in the occipital record, and that, although the frequency in the occipital record in *D* is the same as that in *A*, the per cent time alpha and the amplitude are greater in the former. Amplification constant throughout.

was prolonged and intensified (increased amplitude and regularity), whereas in others it was materially shortened. It is of interest that the second hyperventilation did not result in the appearance of slow waves

8. Rubin, M. A., and Freeman, H.: Brain Potential Changes in Man During Cyclopropane Anesthesia, J. Neurophysiol. **3**:33, 1940.

if the first did not. Conversely, those subjects showing slow activity after the first overventilation always had slowing the second time.

As in the case of alpha activity, no relationship was observed between the appearance of slow waves and the occurrence of somatic sensations. The latter were present many times without the appearance of slow rhythms, and vice versa.

The schizophrenic subjects were far less reactive to hyperventilation than were the nonpsychotic subjects. Only 1 of the group of 35 patients exhibited slowing of his electroencephalogram. On the other hand, slow waves appeared in the electroencephalograms of 19 of the 35 control subjects.

COMMENT

Schizophrenia appears to increase the resistance of the central nervous system to the influence of hyperventilation. In the two groups of 35 subjects each, only 1 schizophrenic patient (3 per cent) had slowing in his electroencephalogram, as compared with 19 normal controls (55 per cent). This is consistent with the general physiologic unresponsiveness of schizophrenic persons.[9]

It might be objected that the number of subjects observed was not large enough for one to obtain reliable differences in the frequency of occurrence of slow waves on hyperventilation. It was found that slow activity occurred in the electroencephalograms of 14 of the first 20 control subjects, whereas only 5 of the next 15 subjects showed slowing. No slowing was seen in the potentials of the first 20 schizophrenic patients, but it did occur in the electroencephalogram of 1 of the next 15 patients. A larger series would undoubtedly establish more accurate percentages of the incidence of slow activity, but it is apparent that the difference between the two groups would not be expected to change appreciably. The difference between normal and schizophrenic subjects becomes more significant when it is borne in mind that the recordings of the two groups were run under the same conditions. Furthermore, a second hyperventilation following within five to ten minutes the end of a preceding overventilation might be expected to have resulted in the appearance of slow waves in the electroencephalograms of as many patients as of normal subjects if it were only a matter of small differences in threshold of the central nervous system to the effects of the first hyperventilation. (In all probability the physiologic effects of hyperventilation last for half an hour or longer.) Actually this was not the case. No subject, whether psychotic or nonpsychotic, showed slow rhythms on the second hyperventilation if he did not do so on the first.

Another factor that could be responsible for the relative absence of slow hyperventilation waves in the electroencephalogram of the schizo-

9. Angyal, A.; Freeman, H., and Hoskins, R. G.: Physiologic Aspects of Schizophrenic Withdrawal, Arch. Neurol. & Psychiat. **44**:621 (Sept.) 1940.

phrenic patient is cooperation. However, only those patients were considered satisfactory who hyperventilated as well as the control subjects. If anything, the patients as a group hyperventilated better than the control group. In fact, it was frequently necessary to keep the patients down to the standard 30 respirations per minute.

The means and the distribution of per cent time alpha were the same in the two groups of subjects, as previously reported.[1] The mean per cent time alpha for the control group was 38.5, and that for the schizophrenic group, 39.9. It follows that the differences in the pre-hyperventilation per cent time alpha is not of importance for the presence or absence of slow activity after hyperventilation.

In the present study a paradoxic situation exists in which one may call the appearance of slow rhythms on hyperventilation normal for nonpsychotic persons and abnormal for schizophrenic persons, since they are uncommon to the latter. Related to this paradox is the observation that also with mild hyperpnea, induced by intravenous injection of sodium cyanide, schizophrenic subjects do not show slow rhythms in their electroencephalograms. However, when a patient is in deep catatonic stupor or in a narcoleptic state, the same degree of hyperpnea results in the appearance of regular, slow waves of large amplitude.[10] Accordingly, as the patients became more abnormal in their behavior their electroencephalograms responded to overventilation more nearly as did those of nonpsychotic persons. It is apparent that labeling these slow potential changes as "normal" or as "abnormal" only causes confusion and contributes nothing to understanding of the phenomenon.

The most reasonable explanation of the appearance of slow waves in the electroencephalogram is that proposed by Gerard and Libet,[11] namely, that they represent a level of synchronization of neurons in the central nervous system. It may then be postulated that in schizophrenia there exists a condition which is unfavorable for synchronization at low frequencies. This is true not only during hyperventilation but under other conditions. For example, when a catatonic patient in deep stupor is given an amount of sodium amytal sufficient to produce drowsiness and concomitant slowing in the electroencephalogram of a nonpsychotic subject, he comes out of stupor and fast, rather than slow, waves appear in his electroencephalogram.[12] Other instances could be cited, all indicating that the schizophrenic patient is frequently "resistive" to factors which produce slow rhythms in nonpsychotic persons.

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10. Rubin, M. A., and Freeman, H.: The Influence of Cyanide on Brain Potentials in Man, J. Neurophysiol. **1**:527, 1938.

11. Gerard, R. W., and Libet, B.: The Control of Normal and "Convulsive" Brain Potentials, Am. J. Psychiat. **96**:1125, 1940.

12. Rubin, M. A.: Slow Potential Changes in the Electroencephalogram and Functional States of the Central Nervous System, Am. J. Physiol. **133**:432, 1941.

The nature of the mechanism involved in the production of slow activity in the electroencephalogram during overventilation is not known. In view of the present report, it is likely that when more is known of the mechanism one will gain further insight into the nature of schizophrenia.

SUMMARY AND CONCLUSIONS

The influence of hyperventilation on the electroencephalograms of 35 schizophrenic patients and of 35 normal control subjects was studied.

A comparison of the two groups revealed no striking differences in the effect of hyperventilation on the amount of alpha activity. However, a second hyperventilation following the first by five or ten minutes did alter the number of persons whose per cent time alpha increased or decreased on overventilation.

Slow waves appeared in the electroencephalograms of 55 per cent of the control group on hyperventilation. The schizophrenic patients, however, were unresponsive in this respect, only 3 per cent (1 patient) showing slow activity. This unresponsiveness of the schizophrenic patients could not be correlated with such factors as age, level of initial per cent time alpha, cooperation or time of day when observed.

It is suggested that some condition exists in schizophrenia which is unfavorable for synchronization of low frequencies, and other instances of the schizophrenic person's unresponsiveness to variables which produce slow rhythms in normal persons are cited.

Knowledge of the mechanism involved in the appearance of slow waves in the electroencephalogram on hyperventilation should contribute to understanding of the nature of schizophrenia.

LIGATION AND RESECTION OF THE SUPERIOR LONGITUDINAL SINUS

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Ligation and resection of the superior longitudinal sinus is a formidable task which must be undertaken in cases of certain tears through the sinus to control hemorrhage or when a meningioma involves the sinus. Meningiomas frequently have their origin of growth from the wall of the sinus, and may invade it often to the extent of completely occluding the lumen of the vessel. In order to effect a permanent cure, the involved portion of the sinus must be removed.

Resection of a sinus previously occluded by a tumor—in effect already resected—would not seem to be dangerous, because the gradual closure of the vessel has permitted sufficient time for an adequate collateral circulation to be slowly established. However, the resection or ligation of a superior longitudinal sinus not already closed is quite another matter. Ligation of a vein invariably leads to temporary venous stagnation and edema in the tissues drained by the vein ligated. If it is a large vein, draining functionally important anatomic parts, the tissue damage induced by this congestion may be irreparable and disastrous. Since the superior longitudinal sinus drains a considerable portion of the cerebral hemispheres, it can be seen that its ligation causes obstructive congestion of the cerebral veins, with resulting edema of that portion of the brain anatomically drained by the collateral veins emptying into the part of the sinus ligated. The extent of the edema is determined by the location of the ligation of the sinus—the more anterior the ligation, the less the interference with the venous drainage.

The venous stagnation must be greatly accentuated when the ligation or resection involves or is posterior to the large venous tributaries—sometimes referred to as the rolandic veins—for these veins are primarily concerned with the drainage of blood from the cortical area in the neighborhood of the central sulcus (O. T. fissure of Rolando). Anatomic variations in the pattern of the arrangement of these veins are common.

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Sometimes there is a single large vein lying in or very near the central sulcus. More commonly there is one large vein with satellite veins anterior and posterior to it. The drawings (fig. 1) of the right and left sides of the same brain show these normal variations. It is important at operation for the surgeon to recognize the general arrangement of

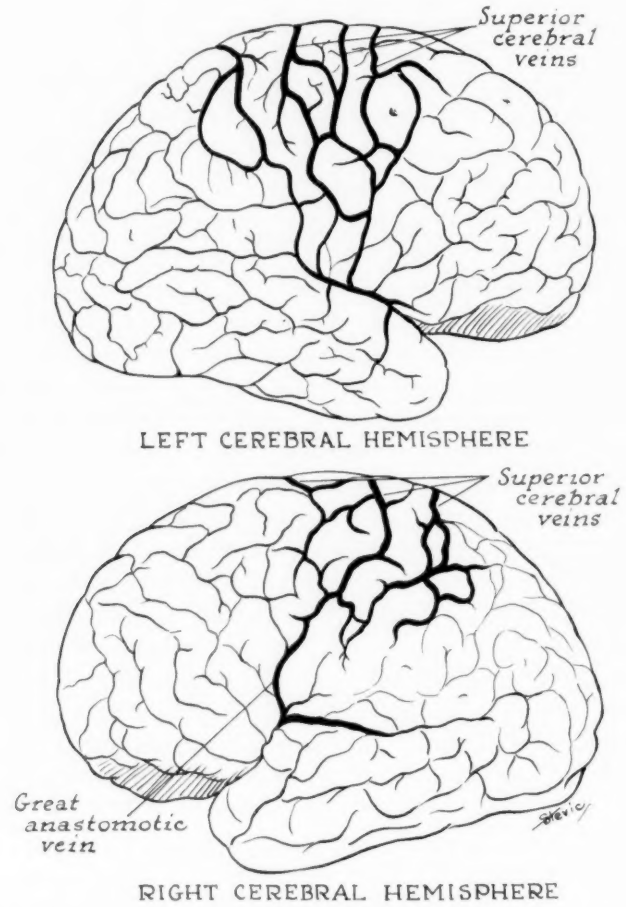

Fig. 1.—Drawings showing the normal variations of the rolandic group of superior cerebral veins on the right and the left side of the same brain.

this vein, or group of veins, in relation to the location of the tumor. Many times it is impossible to determine the actual pattern because the mass is embedded in the very center of these vessels. In the diagrammatic sketches here shown (figs. 3, 4 and 5) the venous tributaries running into the superior longitudinal sinus from the area of the central sulcus are indicated by a single vein. The important relationship of the

tumor to this venous drainage is emphasized. Figure 2 shows the extensive hemorrhagic involvement of the upper motor cortical areas in a case of massive thrombosis of the superior longitudinal sinus. Stopping the flow of blood through the sinus, incident to its ligation or resection, undoubtedly causes similar lesions in the adjacent brain tissue.

A case is reported in this paper in which a patent superior longitudinal sinus was resected, including the rolandic veins, with a fatal ending. In 4 other cases, an unoccluded sinus was ligated anterior to the rolandic veins without ill effect. Five of my cases are cited in

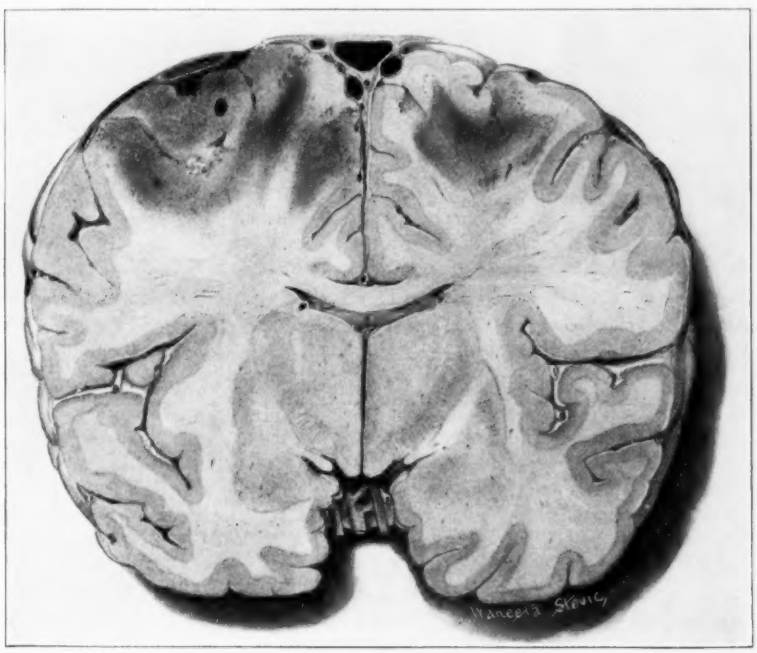

Fig. 2.—Thrombosis of the superior longitudinal sinus and rolandic veins, causing hemorrhagic infiltration of the cerebral cortex.

which the sinus was resected posterior to the rolandic veins, where it had previously been occluded by a tumor.

Dandy,[1] in a recent review of this subject, cited a total of 13 cases, 4 of his own and 9 from other sources, in which the superior longitudinal sinus had been resected for tumor involving it. In 2 of his cases the sinus was removed anterior to the rolandic veins. In his other 2 cases the resection was performed posterior to these veins. Of the other 9

1. Dandy, W. E.: Removal of Longitudinal Sinus Involved in Tumors, Arch. Surg. **41**:244-256 (Aug.) 1940.

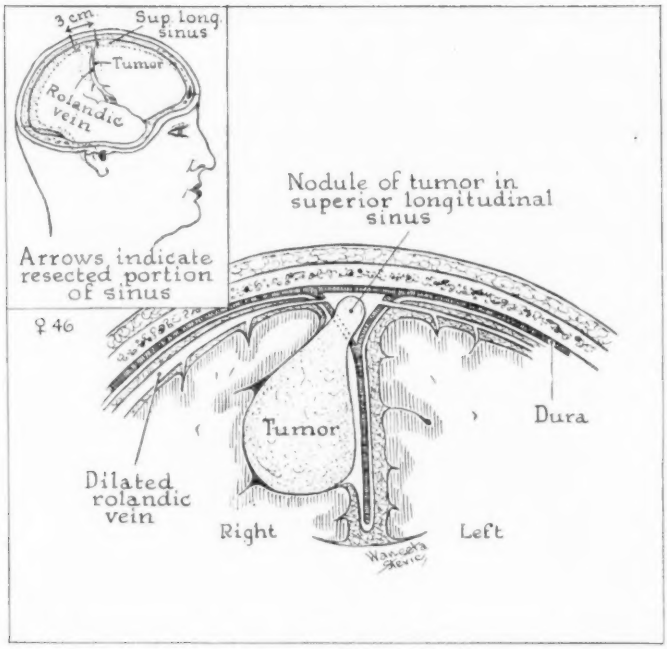

Fig. 3 (case 1).—Partial occlusion of the superior longitudinal sinus just posterior to the rolandic vein. The sinus and veins were resected, and the patient died twelve days after operation.

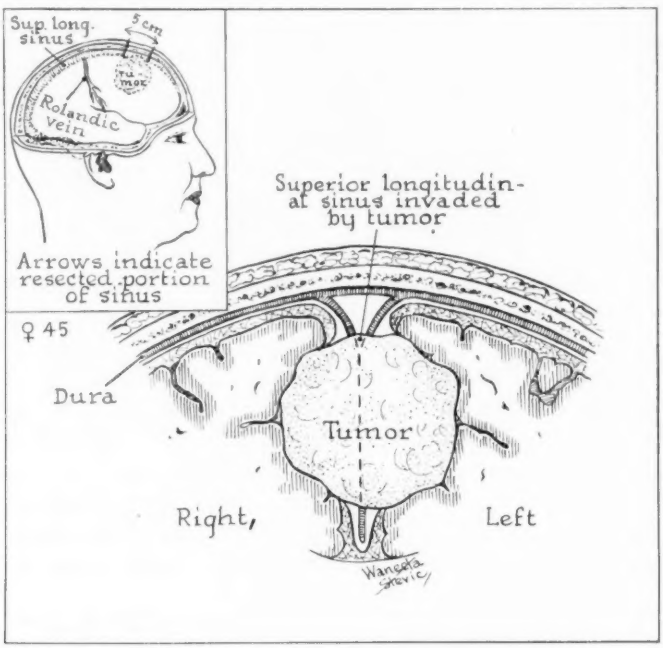

Fig. 4 (case 4).—Portion of the unoccluded superior longitudinal sinus removed with tumor. There was no postoperative effect.

cases reported, resection was made in front of the rolandic veins in 5—Kenyon [2]; Rand [3]; Towne [4]; David, Bissery and Brun,[5] and Horrax, cited by Cushing and Eisenhardt.[6] In 2 cases resection was made back of these vessels—Horrax, Maltby [7] and Tönnis.[8] In 2 cases the portion resected was at the point where the rolandic veins enter the sinus—Rowe [9] and Davidoff.[10] One patient died after operation (Towne [4]) and autopsy showed extensive filling of the unresected part of the sinus with tumor.

Two cases have been reported by daCosta and Adson [11] in which the very anterior end of the sinuses was resected, along with a large parasagittal meningioma, with a successful outcome. The length of the sinus removed was not indicated.

Carlucci [12] doubly ligated the superior longitudinal sinus to control hemorrhage from this vessel when it had been torn by a depressed fragment of bone. The location of the ligation was apparently just anterior to the entrance of the rolandic veins. He stated that on the following day his patient was stuporous and the lower extremities could be moved only slightly. On the second day the legs and arms were spastic. Gradual improvement occurred, until in twelve weeks the patient was walking.

In every instance, except the case reported by Carlucci,[12] a tumor had in all probability already completely occluded the sinus, thereby causing an adequate collateral circulation to be well established prior to the

2. Kenyon, J. H.: Endothelioma of the Brain: Three Years After Operation, Ann. Surg. **61**:106-107 (Jan.) 1915.

3. Rand, C. W.: Osteoma of the Skull: Report of Two Cases, One Being Associated with a Large Intracranial Endothelioma, Arch. Surg. **6**:573-586 (March) 1923.

4. Towne, E. B.: Invasion of the Intracranial Venous Sinuses by Meningioma (Dural Endothelioma), Ann. Surg. **83**:321-327 (March) 1926.

5. David, M.; Bissery, M., and Brun, M.: Sur un cas de méningiome de la faux opere avec succes. Absence de trouble paralytiques apres resection du sinus longitudinal au niveau de l'abouchement des veine rolandiques, Rev. neurol. **1**:725-730 (May) 1934.

6. Cushing, H., and Eisenhardt, L.: Meningiomas, Springfield, Ill., Charles C. Thomas, Publisher, 1938, p. 463.

7. Maltby, G. L.: Resection of Longitudinal Sinus Posterior to the Rolandic Area for Complete Removal of Meningioma, Arch. Neurol. & Psychiat. **42**:1135-1139 (Dec.) 1939.

8. Tönnis, W.: Die Zulässigkeit der Resektion des Längsblutleiters des Gehirns, Deutsche Ztschr. f. Nervenh. **136**:186-190, 1935.

9. Rowe, S. N.: Parasagittal Meningiomas, Am. J. Surg. **43**:138-141 (Jan.) 1939.

10. Davidoff, L. M.: Meningioma: Report of an Unusual Case, Bull. Neurol. Inst. New York **6**:300-305 (Aug.) 1937.

11. daCosta, D. G., and Adson, A. W.: Parasagittal Meningiomas: Report of Cases, Proc. Staff Meet., Mayo Clin. **14**:764-768 (Nov. 29) 1939.

12. Carlucci, G. A.: Injury to Longitudinal Sinus Accompanying Depressed Fracture of the Skull, Am. J. Surg. **45**:120-124 (July) 1939.

resection. One can conclude from these 15 cases that it is possible to resect a portion of the sinus in any location if it has already become plugged by a tumor, without disastrous effects. Dandy concluded his article with the following sentence:

There is, as yet, no available evidence by which it can be known whether the longitudinal sinus can be removed in part before gradually progressive occlusion has occurred.

To support the general impression that the removal of a portion of an unoccluded superior longitudinal sinus at or back of the entrance of

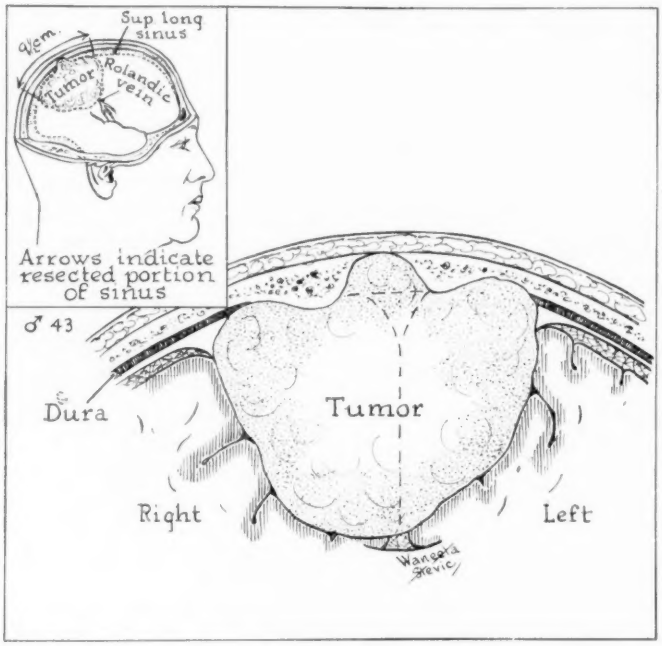

Fig. 5 (case 8).—A meningioma had completely occluded the superior longitudinal sinus at and back of the rolandic veins. Complete removal was accomplished without effect.

the rolandic veins is hazardous, I wish to record the fatal outcome in a case following resection at this point, where a meningioma had invaded the sinus, but had not completely closed it off.

CASE 1 (resection of an unoccluded superior longitudinal sinus at the entrance of the rolandic veins, with fatal outcome).—M. G., a white woman aged 46, was referred by William A. Campbell Jr., of Colorado Springs, Colo., with the complaint of weakness of the left arm and leg and convulsive attacks. The patient was admitted to St. Joseph's Hospital April 25, 1940. One year before she had noticed a slight twitching of the toes of her left foot. Several days after this the toes on the same foot would not move with the same strength as those on the right.

These attacks were repeated frequently, and she was awakened at night by them. Each attack lasted from two to twenty minutes. During the past month, she had had two violent convulsive seizures, in which she was unconscious for twenty minutes. In both the convulsive movements started with jerking of the left foot, then spread upward to involve the left leg and arm and the left side of the face. At no time had she had headache, although she had noticed a "pressure sensation" in the top of her skull which followed immediately the convulsive attack.

Examination.—The patient was mentally alert and cooperative. She walked with a slight limp in the left leg. Strength in this leg was reduced by about one third, and there was questionable weakness of the left arm. She was decidedly left handed. While the patellar and the achilles reflexes were hyperactive on both sides, the responses on the left side were slightly more active than those on the right. The cutaneous sensation was normal. A Babinski sign was elicited on the left side.

On May 4 an encephalographic examination was attempted, and 90 cc. of air was introduced while a like amount of cerebrospinal fluid was removed. Roentgenograms showed no air in the ventricular system. Ventriculographic studies, which were immediately performed, showed no deviation of the ventricles from the normal.

Operation (May 11).—A preoperative diagnosis of a small parasagittal neoplasm was made, with the greater part of the mass in the right motor foot center. A bone flap was turned down over the right motor area close to the midline, extending up to the very edge of the superior longitudinal sinus. When the dura was opened, the cerebral hemisphere was not tense. A single rolandic vein was so much enlarged that at first I suspected it might be a venous angioma. The vessel was followed to the midline, inasmuch as it occurred to me that quite possibly there was some obstruction to the outflow of this vein into the superior longitudinal sinus at the place where the vein entered the sinus. At this point there was observed a solid tumor attached to the falx and the superior longitudinal sinus and well hidden by the overlying cortex. In order to expose the mass, it was necessary to coagulate and cut the large rolandic vein as it entered the sinus. The cerebral hemisphere was retracted from the falx, and a tumor 3.5 cm. in diameter was observed to be tightly adherent to the superior longitudinal sinus by a base approximately 1 cm. in diameter (fig. 3). It was easily peeled from the sinus wall, leaving a small, rough spot. After removal of the tumor, its base was thoroughly inspected, and a small nodule could be felt inside the sinus. In order to make sure of this, a small bone flap was turned back across the midline so as thoroughly to expose the sinus for a length of 7 cm. A dural flap was made on the left side to inspect the left rolandic vein and to permit palpation of the sinus between the thumb and forefinger. It was thought that a small nodule inside the sinus was large enough to occlude this vessel completely. It was realized that this segment of the sinus must be removed completely in order to effect a permanent cure. The left rolandic vein and two smaller veins were coagulated and cut from the sinus. A suture was placed around the sinus about 1.5 cm. anterior and posterior to the tumor mass, so that approximately 3 cm. of it was ligated and removed. The defect left in the dura was closed with Cargile membrane. The bone flap was wired in place, and the galea was closed with interrupted silk sutures. There was little bleeding throughout the procedure. The patient's condition at the completion of the operation was excellent. The pulse rate was 90; the blood pressure was 120 systolic and 80 diastolic, and there was no evidence of shock.

The piece of longitudinal sinus removed at the operation was opened by cutting longitudinally through its superior wall. To my amazement, there was found

sufficient room around the tumor mass for the venous blood to pass readily. The The tiny tumor nodule, approximately 7 mm. in diameter, occluded about one-half the lumen of this vessel.

Postoperative Course.—On the second day the general condition was excellent. The temperature was 100 F. and the pulse rate 95. The patient talked well. On the third day her condition was good; she talked easily and was comfortable; the temperature was 100 F. and the pulse rate 80. On the fourth day it was noticed that her right leg and arm were weak. Her speech was good; the temperature was still 100 F. and the pulse rate 70. On the fifth day the temperature was 101 F. and the pulse rate 85; the right side was almost completely paralyzed, and she was stuporous and slightly irrational. On the sixth day the temperature was 102 F. and the pulse rate 90; the right side was completely paralyzed; speech was good, although she was irrational and drowsy. On the seventh to twelfth day the temperature and pulse rate gradually rose, the temperature fluctuating anywhere from 104 to 99 F., with a pulse rate of 150 per minute. The patient was irrational, although able to talk in her confusion; after this, she became stuporous and unconscious. All of the time she was able to move her left extremities, and there remained complete paralysis of the entire right side of the body. She died on the twelfth postoperative day. Autopsy was not permitted.

COMMENT

It is an interesting observation that this patient's postoperative paralysis was on the right side of the body, although the tumor was in the right cerebral hemisphere. The mechanism of this paralysis can be rationalized on the assumption that the single right rolandic vein, which drained most of the right motor cortex, was already occluded by the pressure of the tumor growth which was directly beneath it. This had permitted adequate collateral circulation to develop slowly in the motor area of the right cerebral hemisphere. On the left side, it was necessary to ligate a normal rolandic vein, with two small veins close to it which ran directly into the sinus at the point of the resection. The serious condition of this patient was brought about by the ligation of the left rolandic vein, which caused sudden stagnation of the blood flow with massive edema of the left cerebral hemisphere. The fact that she was left handed and that she was able to talk right up to the last day without interference with speech indicates that there was no massive damage to the right cerebral hemisphere from the ligation of the right rolandic vein and the resection of the sinus.

The same phenomenon of more extensive postoperative paralysis in the noninvaded cerebral hemisphere was noted in case 9, in which the location of the tumor was comparable to that in this case, although the sinus was completely occluded, No note was made of a similar occurrence in the cases of the other tumors resected, and there probably was none, for in these cases the tumor had invaded the opposite hemisphere and had already thrombosed the large cortical veins. Therefore, no physiologic disturbance, as far as the motor areas were concerned, would have been expected.

In 4 of my cases a patent superior longitudinal sinus was ligated anterior to the rolandic veins.

Case 2.—The sinus was closed by a muscle fragment and silk sutures because of hemorrhage from a perforating wound.

Case 3.—Four centimeters of the sinus was resected on the suspicion that a meningioma had invaded it.

Case 4.—Four centimeters of the sinus was removed because the tumor had invaded the falx and the lower part of the sinus (fig. 4).

Case 5.—The meningioma was attached to the base of the skull and filled the anterior fossae. It was necessary to do a simple ligation and section of the sinus in order to approach it.

Cases 2, 3, 4 and 5 and the one reported by Carlucci seem to indicate that it is possible to resect or ligate with safety an unoccluded superior longitudinal sinus anterior to the rolandic veins.

In 4 of my cases the sinus was safely resected at a location which included the rolandic veins and a part of the sinus back of this spot, while in a single case the resection was performed between the rolandic veins and the torcular Herophili. In each instance, however, the lumen of the vessel had been completely occluded by a tumor growth.

Case 6.—The patient had a huge meningioma with a large osteoma overlying it. The bone had to be discarded; the tumor, with 12 cm. of the sinus, was resected and the bone defect filled with a stainless steel plate.

Case 7.—The meningioma was observed to invade the sinus but not to occlude it. Two and a half years later it had recurred and occluded the sinus. Six and a half centimeters of the sinus and the tumor were removed at the second operation.

Case 8.—A huge tumor just anterior to the torcular Herophili was resected, with 9.5 cm. of the sinus (fig. 5).

Case 9.—A small meningioma had completely occluded the sinus at the rolandic veins. Recovery was uneventful except for temporary profound paralysis on the same side as the tumor, thought to be due to ligation of the rolandic veins draining a normal mortor cortex. The same profound paralysis of the normal side was observed in case 1.

Case 10.—A tumor nodule, which had completely occluded the sinus, was withdrawn from it. The hole was closed by ligating the sinus.

Summary of Cases.—Ten cases are reported in which I either resected a portion of or ligated the superior longitudinal sinus. In 4 of these cases the operation was performed anterior to the rolandic venous outflow. In none of these cases had the sinus become occluded before the operation, and in not a single case was there any sign of the closure.

In 6 cases the sinus was resected at or posterior to the rolandic veins. Five patients of this group lived without suffering disastrous results from the operation. One—the patient with the smallest tumor in the whole group, and the only one in whom the sinus was not occluded—died after the resection.

CONCLUSIONS

From this review, it seems logical to conclude that the superior longitudinal sinus can be ligated or resected safely anterior to the point where the rolandic veins enter the sinus without regard to whether or not a tumor is compressing or occluding this structure. It also appears safe to remove a portion of the sinus at or back of the rolandic veins provided the sinus has already been slowly occluded by a tumor growth.

The case reported here, with death following resection of an unoccluded superior longitudinal sinus at the entrance of the rolandic veins, would indicate that the procedure is incompatible with life, although similar case reports are needed before a positive assertion of this belief is warranted.

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ABSTRACT OF DISCUSSION

Dr. James L. Poppen, Boston: Dr. Jaeger has presented an important paper. It has long been known that ligation of either of the rolandic veins may have dire consequences, and I, for one, fear surgical occlusion of the rolandic vein. However, I have no hesitancy in ligating any portion of the longitudinal sinus anterior to the rolandic vein when it is deemed necessary. Ligating a longitudinal sinus already occluded by tumor in the rolandic vein seems perfectly safe. One must remember, however, that the rolandic vein does not always empty directly into the longitudinal sinus but may drain into the venous spaces of the dura several millimeters, and at times as much as 1 cm., lateral to the longitudinal sinus. These spaces may pass posteriorly or anteriorly for a considerable distance before they empty into the longitudinal sinus. It is also true that the cortical veins empty not only into the longitudinal sinus but into the venous spaces of the falx and the inferior sagittal sinus, thus creating an accessory region for drainage which may be adequate for the venous return if the rolandic vein ligated.

Dr. Jaeger mentioned that in case 7, because of the fatal outcome, he felt he had used poor judgment in extirpating the tumor. I, for one, do not like to divide the removal of a parasagittal or a sagittal meningioma into more than one operation unless absolutely necessary. Certainly, to wait for occlusion of the longitudinal sinus by tumor does not seem logical when in most cases a sufficient amount of the sinus can be saved for adequate drainage.

If the tumor has invaded the lateral surface of the sinus, by occluding a portion of it and resecting the lateral margin one can still have adequate blood supply. However, one should first open the dura over the opposite hemisphere. For that reason, in the extirpation of these tumors it is important that the bone be removed from the sinus and for several centimeters beyond. This permits inspection of the veins on the opposite side, and many times reveals that the draining vessels are behind the area that the tumor invades or that the venous lacunas of the dura in the region next the sagittal sinus are sufficiently large to drain the opposite hemisphere. After freeing the tumor, with the exception of its attachment to the longitudinal sinus, one can then elevate it and, by the use of curved clamps along the lateral margins of the sagittal sinus, enlarge the sinus for adequate drainage. Then, by suturing with interrupted black silk or continuous black silk, an adequate channel will be left.

One must be cautious, of course, in surgical procedures on the sagittal sinus in the rolandic area; however, regardless of whether or not the sinus is completely occluded by the tumor, it can be removed successfully in one stage without permanent serious consequences.

DR. J. W. WATTS, Washington, D. C.: I have never ligated a longitudinal sinus. It has always seemed a formidable procedure, but after hearing this paper I am sure that often more damage is done to the brain by retracting the cerebral hemisphere than would be done to the circulation by ligating the sinus.

The emphasis in the paper has been placed on hemiplegia which has resulted from ligation of the sinus. I should like to ask Dr. Jaeger whether he has found any signs of involvement of the frontal lobe, such as great confusion, disorientation or drowsiness, after ligating the sinus in front of the fissure of Rolando. When the sinus was ligated posterior to the fissure of Rolando, was hemianopia or analgesia noted?

Since Dr. Jaeger has been able to show that the sinus can be ligated anterior to the rolandic vein without serious consequences, should that be done or should the frontal lobe be removed in order to obtain exposure to remove a meningioma in the olfactory groove? I should like to know his opinion of the relative advantages and disadvantages.

DR. J. RUDOLPH JAEGER, Denver: I appreciate the discussions of Dr. Poppen and Dr. Watts.

In connection with the case that ended fatally, I should in a similar instance bring a portable x-ray machine into the operating room and take a lateral roentgenogram while injecting sodium iodide into the sinus. In this way I could tell if it had been completely occluded or not. I do not know of any better way of preventing a fatality than to permit the tumor to grow to such size that one feels fairly certain it has occluded the sinus before resecting the growth. That is what I did in 1 of the cases reported.

Dr. Poppen's suggestion as to the preservation of a tiny channel in the sinus if possible is important. Many times there is no question but that the tumor is attached far out into the lateral lacunas. Here, the lacunas can be resected with the tumor, and a tiny channel can be preserved that will be adequate to take care of the circulatory needs of the cortex. In 1 case reported, there was a large bilateral tumor of the frontal lobe with mental symptoms. The tumor was a large, flat meningioma that covered a huge area of the frontal lobes. One can appreciate that damage to the brain structure must be extensive in removing such a mass. In this instance the mental weakness was aggravated.

I have not observed the complication of hemianopia. After the bone has been turned well back to expose the sinus and the dura has been opened, the cortex can be retracted without great pressure on it. There seems to be adequate room around the tumor to work provided too much of the dura is not opened and the brain seems to lie rather loosely inside the skull. It is amazing how much immediate physiologic damage is done to the motor area of the brain around the tumor and how complete can be the recovery from the resulting extensive paralysis.

TRUE FATTY DEGENERATION IN SENSORY NEURONS OF THE AGED

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AND
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The problems of aging and their correlation with senile changes as observed within the nervous system have been the object of extensive investigation. When interpreting microscopic observations on the senile nervous system one must bear in mind the following questions: 1. Do such structural alterations represent a normal senile involution of the nerve cell, or are they secondary to infectious processes, malnutrition and changes in blood supply?

2. Are these changes truly the result of antemortem degeneration, or do they represent postmortem autolysis?

3. Are they technical artefacts, such as shrinkage due to fixation in an acid solution of formaldehyde or to prolonged fixation in alcohol or vacuolation resulting from indiscriminate use of water at autopsy?

4. What is the nature of this senile change when observed with a variety of technics?

These and similar considerations account for many differences of opinion.

One of us (R. C. T.) [1] has described a fatty degenerative process in the sensory neurons of man which appears to be correlated with age. The principal features of this process are initial clumping of Nissl chromatin and subsequent destruction of the neurofibrillar reticulum in the periphery of the cytoplasm. This area, usually in the region of the axon hillock, consists of minute vacuoles and appears "foamy" when studied with silver impregnation technics. Progressive cytoplasmic degeneration with fusion and coalescence of vacuoles ultimately leads to complete destruction of some cells and their processes. Specific fat stains were not applied in this early investigation, so that the presence of lipoid was not definitely reported until later.[2]

From the Department of Anatomy, Columbia University College of Physicians and Surgeons.

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2. Truex, R. C., and Zwemer, R. L.: Anat. Rec. **79** (supp. 2):60, 1941.

Similar forms of degeneration accompanied by lipoidal pigments and vacuolation associated with the aging process have been observed in various neurons by numerous investigators.[3] On the other hand, many authors have interpreted vacuolation of neurons as an artefact resulting from postmortem autolysis, improper fixation or faulty technic.[4]

3. Hodge, C. F.: Changes in Ganglion Cells from Birth to Senile Death: Observations on Man and Honeybee, J. Physiol. **17**:129, 1894. Pilcz, A.: Beitrag zur Lehre von der Pigmententwickelung in den Nervenzellen, Arb. Inst. f. Anat. u. Physiol. **3**:123, 1895. Rosin, H.: Ein Beitrag zur Lehre vom Bau der Ganglienzellen, Deutsche med. Wchnschr. **22**:495, 1896. Rosin, H., and Fenyvessy, B.: Ueber das Lipochrom der Nervenzellen, Virchows Arch. f. path. Anat. **162**:534, 1900. Lord, J. R.: A New Nissl Method: Normal Cell Structure and the Cytological Changes Terminating in Fatty Degeneration, J. Ment. Sc. **64**:693, 1898. Sander, M.: Untersuchungen über die Altersveränderungen im Rückenmark, Deutsche Ztschr. f. Nervenh. **17**:369, 1900. Mühlmann, M.: Ueber die Veränderungen der Nervenzellen im verschiedenem Alter beim Meerschweinchen, Anat. Anz. **19**:377, 1901. Obersteiner, H.: Ueber das hellgelbe Pigment in dem Nervenzellen und das Vorkommen weiterer fettähnlicher Körper im Zentralnervensystem, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **10**:245, 1903. Harms, W.: Morphologische und experimentelle Untersuchungen an Alter den Hunden, Ztschr. f. Anat. u. Entwcklngsgesch **71**:319, 1924. Flügel, F. E.: Quelques recherches anatomiques sur la dégénérescence sénile de la moelle épinière, Rev. neurol. **34**:618, 1927. Stankiewitsch, E.: Vom Lebensalter abhängige Nervenzellenveränderungen beim Menschen, Ztschr. f. Zellforsch. **22**:80, 1934. Stern, K.: Beitrag zur Histopathologie des senilen Rückenmarks, Ztschr. f. d. ges. Neurol. u. Psychiat, **155**:543, 1936. Csermely, H.: Seltenere Zellveränderungen beim Dementia senilis, Arch. f. Psychiat. **109**:206, 1938. Andrew, W.: Cytological Changes in Senility in the Trigeminal Ganglon, Spinal Cord and Brain of the Mouse, J. Anat. **75**:406, 1941.

4. (*a*) Schultz, R.: Ueber artificielle, cadaveröse und pathologische Veränderungen des Rückenmarks, Neurol. Zentralbl. **2**:529, 1883. (*b*) Kreyssig, F.: Ueber die Beschaffenheit des Rückenmarks bein Kaninchen und Hunden nach Phosphor und Arsenikvergiftung nebst Untersuchungen über die normale Struktur desselben, Virchows Arch. f. path. Anat. **102**:286, 1885. (*c*) Trzebinski, S.: Einiges über die Einwirkung die Härtungsmethoden auf die Beschaffenheit der Ganglienzellen im Rückenmark der Kaninchen und Hunde, ibid. **107**:1, 1887. (*d*) Ewing, J.: Studies on Ganglion Cells, Arch. Neurol. & Psychopath. **1**:263, 1898. (*e*) Barbacci, O., and Campacci, G.: Sulle lesioni cadaveriche delle cellule nervose, Riv. di pat. nerv. e ment. **2**:337, 1897. (*f*) Colucci, C.: Sulla morfologia e sulle valore delle parte constituenti la cellula nervosa, Ann. di neurol. **14**:145, 1896. (*g*) Held, H.: Beiträge zur Structur der Nervenzellen und ihrer Fortsätze, Arch. f. Anat. u. Physiol (Anat. Abt.) **21**:204, 1897. (*h*) Neppi, A.: Sulle alterazioni cadaveriche della cellule nervose rilevabili col metodo di Nissl, Riv. di pat. nerv. e ment. **2**:152, 1897. (*i*) Hoch, A.: Nerve Cell Changes in Somatic Disease, Am. J. Insanity **55**:231, 1898. (*j*) Orr, D., and Rows, R. G.: The Nerve Cells of the Human Posterior Root Ganglia and Their Changes in General Paralysis of the Insane, Brain **24**:286, 1901. (*k*) Carazzi, D.: Artefatti, pigmento e vacuoli nelle cellule die gangli spinali di mammiferi, Monitore zool. ital. **18**:235, 1907. (*l*) Tebelis, F.: Ueber Fixierungsartefakte in Zentralnervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **162**:767, 1938.

Lenhossek [5] expressed the belief that cytoplasmic vacuoles were normal cell constituents, whereas Takeda [6] stated that vacuole formation was responsible for the production of atypical fenestrated cells. Others [7] have concluded that pigmentation in the neuron denotes functional activity rather than decadence and senility. Still others [8] have given special pathologic significance to comparable changes in the Nissl pattern (chromatolysis) and vacuole formation.

A more extensive study seemed desirable in view of these conflicting reports. Since the earlier investigation [1] did not distinguish simple vacuolation from true fatty degeneration or antemortem change from postmortem autolysis, these points are dealt with particularly in the present study.

MATERIAL AND METHODS

Gasserian, spinal and sympathetic ganglia from human material (ages 45, 51 and 76 years) were obtained at autopsy from both sides of the body within three hours after death. These ganglia were fixed in a 4 per cent concentration of calcium carbonate–neutralized solution of formaldehyde U. S. P. for twenty-four hours.

One ganglion from each of the specimens was partially cut on a freezing microtome (20 microns) and the sections were stained with either sudan III or scarlet red. Both series were later counterstained with iron hematoxylin and

5. von Lenhossek, M.: Der feinere Bau des Nervensystems, Berlin, Gustav Fischer, 1895, pp. 170-171.

6. Takeda, G.: Ueber die gefensterten Zellen und die Zellen mitt Vakuolen im Ganglion semilunare, Folia anat. jap. **3**:17, 1925.

7. Shäfer, E. A.: The Nerve Cell Considered as the Basis of Neurology, Brain **16**:134, 1893. Altschul, R.: Ueber das sogenannte "Alterspigment" der Nervenzellen, Virchows Arch. f. path. Anat. **301**:273, 1938.

8. (*a*) Leyden, E.: Klinik der Rückenmarkskrankheiten, Berlin, August Hirschwald, 1874, pp. 75-76. (*b*) Fleming, R. A.: Notes on Two Cases of Peripheral Neuritis with Comparative Results of Experimental Nerve Degeneration and Changes in Nerve Cells, Brain **20**:56, 1897. (*c*) Meyer, A.: Demonstration of Various Types of Changes in the Grand Cells of the Paracentral Lobule, Am. J. Insanity **54**:221, 1897. (*d*) Wintrobe, M. M.; Mitchell, D. M., and Kolb, L. C.: Sensory Neuron Degeneration in Vitamin Deficiency, J. Exper. Med. **68**:207, 1938. (*e*) Wintrobe, M. M.; Miller, J. L., and Lisco, H.: The Relation of Diet to the Occurrence of Ataxia and Degeneration in the Nervous System of Pigs, Bull. Johns Hopkins Hosp. **67**:377, 1940. (*f*) Mitchell, D.: Spinal Cord Degeneration Produced by Dietary Means, Brain **64**:165, 1941. (*g*) Sabin, A. B., and Aring, D.: Visceral Lesions in Infectious Polyneuritis, Am. J. Path. **17**:469, 1941. (*h*) Wintrobe, M. M.; Muschatt, C.; Miller, J. L.; Kolb, L. C.; Stein, H. J., and Lisco, H.: The Prevention of Sensory Neuron Degeneration in the Pig with Special Reference to the Role of Various Liver Fractions, J. Clin. Investigation **21**:71, 1942.

mounted in glychrogel.[9] The remainder of the partially cut ganglion was dehydrated and embedded in paraffin with the control ganglion of the opposite side. Serial sections cut at 10, 12 and 15 microns from both ganglia were then stained with the silver-protargol and cresyl violet technics for purposes of comparison.

In order to insure immediate fixation and eliminate postmortem autolysis, normal senile animals were perfused with a 4 per cent concentration of neutral solution of formaldehyde U. S. P. while under profound ether anesthesia. Two cats (ages 6 and 14 years) and 2 white rats (male litter mates 102 weeks of age) were perfused in this manner. The spinal and gasserian ganglia were removed immediately and, after twenty-four hours of continued fixation, were cut and stained in the same manner as the human material. In the case of the 6 year old cat, the ganglia of one side were stained with osmic acid.

OBSERVATIONS

In all of the sensory ganglia we observed a uniform appearance of fat droplets in the cell body with the application of specific stains. The lipoidal accumulations were usually located in the periphery of the cell cytoplasm in the region of the axon hillock, although dispersed and perinuclear distributions were not uncommon.

Osmic acid preparations demonstrated clearly the early appearance of fat, which stood out in sharp contrast to the remainder of the cytoplasm as discrete, black, oval or angular bodies (fig. 1 *A*). Late and terminal stages of the degenerative process could not be shown adequately with this technic (fig. 1 *B*), as in the larger accumulations of lipoid all the osmic acid is not reduced. It should also be pointed out from studies on adult cats not used in this series that if the ganglia were treated previously with alcohol and ether to remove fat, the osmic acid action was not obtained.

Preparations of frozen sections with sudan III and scarlet red demonstrated the lipoid as light yellow and orange droplets respectively. In the initial stages the dispersed individual droplets were easily recognized (fig. 2 *A*), whereas in the later stages the fat appeared in compact masses of superimposed droplets (fig. 2 *B*).

In cresyl violet preparations the region of the cytoplasm which was occupied by the lipoid contained no demonstrable Nissl bodies. Thus it appeared as a light area filled with fine, dustlike particles of debris and was sharply delimited from the adjacent normal cytoplasm.

Although the histologic picture was identical in the human and the animal specimens, the fat droplets were no longer in evidence after

9. Glychrogel contains, in 100 cc., 20 cc. glycerin, 3 Gm. granulated gelatin, 0.2 Gm. chrome alum (chromium and potassium sulfate) and 80 cc. distilled water. Its preparation has been described by Zwemer (A Method for Studying Adrenal and Other Lipoids, Anat. Rec. **57**:41, 1933).

staining by the silver-protargol method. Here one saw only minute vacuoles (fig. 3 *A*), since the fat had been extracted (dissolved) in the alcohol-xylene treatment of paraffin embedding. In more advanced

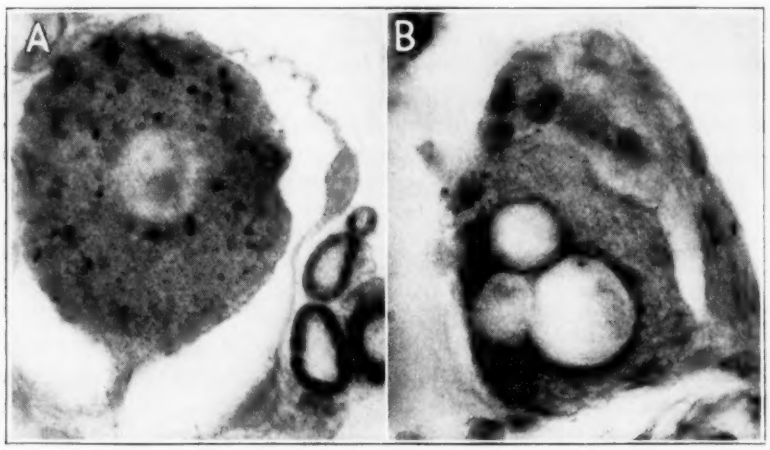

Fig. 1.—*A*, early appearance of osmicated bodies in the cytoplasm of a gasserian ganglion cell of a cat 6 years old.

B, late stage of fatty degeneration in a gasserian ganglion cell of the same cat as that from which *A* was taken. Note vacuoles of fat in which osmium has been reduced at the periphery.

Osmic acid; × 860.

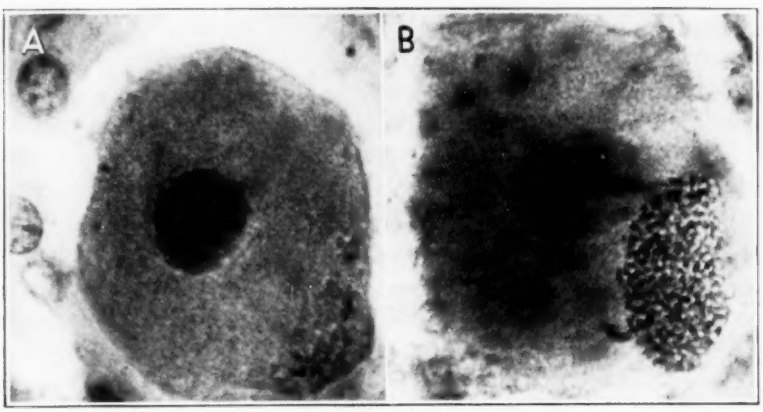

Fig. 2.—*A*, early appearance of fat droplets as demonstrated in frozen sections of the gasserian ganglion of a cat 14 years old.

B, advanced stage of fatty degeneration in the same cat as that from which *A* was taken. Note demarcation from adjacent normal cytoplasm.

Sudan III; × 640.

stages of the degenerative process, in which coalescence of smaller vacuoles had occurred with this method, one observed the unilocular appearance, as shown in figure 3 *B*. These serial silver preparations of controlled human and animal ganglia demonstrate all the transitional stages and variations described previously in man.[1]

Studies of the human sympathetic ganglia, in contrast to the sensory ganglia, showed in the same 3 specimens a pronounced decrease in the number of efferent cells involved. Thus, only an occasional sympathetic cell showed fatty degeneration, whereas it was rare to find a sensory cell entirely devoid of fat droplets.

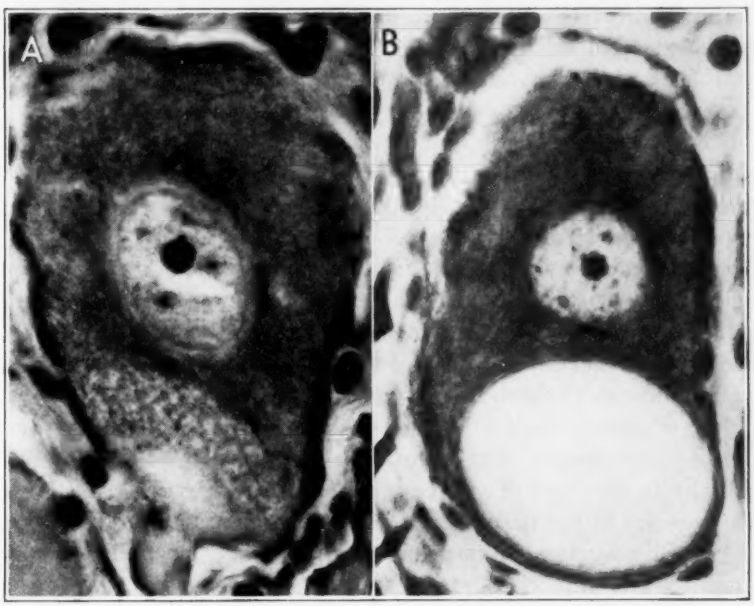

Fig. 3.—*A*, early degeneration in the gasserian ganglion of a cat 14 years old as observed with the silver-protargol stain after extraction of fat by organic solvents during embedding. × 466.

B, unilocular vacuole from the same specimen as that from which the photographs in figures 2 *A* and *B* and 3 *A* were taken. This vacuole resulted from coalescence of smaller vacuoles. × 466.

COMMENT

As a result of these observations, we feel justified in stating that true fatty degeneration occurs in afferent neurons. This represents a gradual antemortem alteration, as confirmed by fresh autopsy specimens and animal experiments.

We are well aware of the changes which may be induced in nerve cells by delayed fixation; however, all vacuolation of neurons does not

represent cadaveric changes, as has been firmly asserted by certain investigators.[10] Ample proof lies in the demonstration of actual fat droplets by specific stains, whereas a different technic (silver-protargol) with sections cut from the same block will show such cytoplasmic destruction as that evidenced by vacuoles. The fatty changes we have described in this paper should not be confused with senile fatty plaques described in other studies.[11]

It is unknown why sensory cells are so extensively involved, while the sympathetic neurons escape this degenerative process. Whether the efferent cells are more resistant or such destructive changes are expressed only much later are merely conjectures.

The fat droplets we have described are soluble in the organic solvents used before paraffin embedding. They stain yellow to orange with sudan III and scarlet red and reduce osmic acid. They are possibly phosphatides with unsaturated fatty acids in their molecules.

No confusion should exist between these accumulations and pigmentary deposits of lipochrome and lipofuchsin, which are present after ordinary paraffin and pyroxylin embedding technics and which require no special stain to make them visible.

Experimental studies in this field are still too few to warrant definite conclusions. The relation of changes in the gasserian ganglia when obtained from edentulous specimens, as well as the role of diet [12] and vascular disturbances [13] in effecting alterations in the spinal and gasserian ganglia, must await further investigation.

This wholesale destruction of sensory neurons and their processes after the fourth decade [1] may be correlated with a clinical loss of vibratory sensitivity in corresponding age groups.[14] Further evidence of this loss is to be found in the morphologic decrease in the number of peripheral and central processes of these neurons with age, as noted in recent studies.[15] The fatty changes are seen in sensory cells of normal aged

10. Kreyssig.[4b] Trzebinski.[4c] Ewing.[4d] Held.[4g]

11. Rizzo, C.: Contributo all'istologia patologica della senilità, Riv. di pat. nerv. e ment. **29**:295, 1924. Dias, A. A.: Untersuchungen über die senilen Plaques, Ztschr. f. d. ges. Neurol. u. Psychiat. **128**:23, 1930.

12. Wintrobe, Mitchell and Kolb.[8d] Wintrobe, Miller and Lisco.[8e] Mitchell.[8f] Wintrobe and associates.[8h]

13. Alexander, L., and Bergmann, L.: Vascular Supply of the Spinal Ganglia, Arch. Neurol. & Psychiat. **46**:761 (Nov.) 1941. Bergmann, L.: Studies on the Blood Vessels of the Human Gasserian Ganglion, Anat. Rec. **82**:609, 1942.

14. Pearson, G. H. J.: Effect of Age on Vibratory Sensibility, Arch. Neurol. & Psychiat. **20**:482 (Sept.) 1928.

15. Duncan, D.: Incidence of Mild Degrees of Atrophy in the Fasciculus Gracilis, Arch. Path. **26**:664 (Sept.) 1938. Corbin, K. B., and Gardner, E. D.: Decrease in Number of Myelinated Fibers in Human Spinal Roots with Age, Anat. Rec. **68**:63, 1937. Gardner, E.: Decrease in Human Neurons with Age, ibid. **77**:529, 1940. Cottrell, L.: Histologic Variations with Age in Apparently Normal Peripheral Nerve Trunks, Arch. Neurol. & Psychiat. **43**:891 (June) 1940.

specimens. Recognition of this picture as noted in microscopic preparations will eliminate its erroneous interpretation as a pathologic criterion in explaining observed antemortem clinical conditions.

SUMMARY

A study of aged human and animal sensory ganglion cells shows widespread fatty degeneration. This change is demonstrable as actual fat droplets when specific stains are applied to frozen sections, but appears as vacuoles in paraffin-silver preparations.

In the efferent sympathetic cells this destructive process is not as prevalent as in the afferent neurons. The reason for this difference is unknown.

Immediate fixation of the material of experimental animals precludes the possibility that these changes in the nerve cells represent postmortem autolysis. The alterations are therefore valid antemortem changes.

Variations in the appearance of the lipoidal accumulations with different histologic technics are described. A recognition of these differences will eliminate erroneous interpretations of their pathologic significance.

The general literature pertaining to the problem is reviewed and discussed.

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Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

DEVELOPMENT OF THE AFFERENT COMPONENTS OF THE FACIAL, GLOSSOPHARYNGEAL AND VAGUS NERVES IN THE RABBIT EMBRYO. DONALD L. KIMMEL, J. Comp. Neurol. **74**:447 (June) 1941.

Thirty-five embryos of rabbits, ranging in age from the 11 day stage to full term, were studied in both the transverse and the sagittal plane, and their brains were compared with those of animals 1 week old and of adults. In the 11 day embryos a primitive representation of all the ganglia associated with the facial, glossopharyngeal and vagus nerves in the adult was present. By the thirteenth day central processes of the cells of the geniculate ganglion were seen terminating within the nucleus of the spinal root of the fifth nerve, within the prevagal portion of the fasciculus solitarius and in a small cell nucleus in the region of the internal genu of the facial nerve. The central processes of ganglion cells of the glossopharyngeal and vagus nerves also ended partly in the spinal root of the fifth nerve, but the major portion of both nerves entered the fasciculus solitarius. Each nerve also contained fibers which terminated within nuclear groups located near the floor of the fourth ventricle, such as the nucleus praepositus, the nucleus intercalatus, the nucleus eminentiae medialis and the nucleus of Roller. Fibers originating in the nucleus of the mesencephalic root of the fifth nerve were followed to the level of the facial nerve, where they divided dichotomously. One process passed out of the brain stem with the facial nerve, and the other passed medially and ended in synaptic relation with the cells of the primitive motor nucleus of the facial nerve. Other fibers which appeared to originate within the nucleus of the mesencephalic root of the fifth nerve at all levels caudal to the decussation of the fourth nerve seemed to join the rubrospinal and rubrobulbar fibers. This relationship suggests the possibility that all of the motor nuclei of the lower portion of the brain stem may be functionally related to the nucleus of the mesencephalic root of the trigeminal nerve through cell processes which course to motor nuclei in company with extrapyramidal fibers.

FRASER, Philadelphia.

EXPERIMENTAL STUDIES ON THE DEVELOPMENT OF THE CORNEAL REFLEX IN AMPHIBIA. JERRY J. KOLLROS, J. Exper. Zool. **89**:37 (Feb.) 1942.

The time of appearance of the corneal reflex in embryonic development was determined in 12 species of amphibians, and the adults of 4 additional species were likewise studied. This reflex, which consists of withdrawal of the bulb into the orbit, lifting of the nictitating membrane and closure of the lids, was elicited by touching the cornea or the adjacent skin with a human hair mounted in a glass tube. The reflex is usually not present in larvae but appears during the metamorphic climax or shortly before. Each species has its own period for the appearance of the reflex. Urodeles and anurans differ with respect to the time of onset and the spread of the reflexogenous area. In urodeles the period of onset of the reflex may be earlier than in anurans and may vary with the rate of growth as determined by nutrition, and the reflexogenous zone is larger. Separate parts of the reflex arc are capable of functioning in midlarval stages, long before the reflex can be elicited by stimulation of the cornea. The sudden appearance of the reflex, therefore, may depend on changes in brain centers. WYMAN, Boston.

ARHINENCEPHALY WITH INCOMPLETE SEPARATION OF THE CEREBRAL HEMISPHERES. G. W. T. H. FLEMING and R. M. NORMAN, J. Ment. Sc. **88**:341, 1942.

Fleming and Norman report a case of arhinencephaly associated with incomplete division of the frontal and parietal lobes. The interhemispheric connections were derived from the cingulate gyri, and at the frontal pole took the form of interdigitating gyri, which gave an appearance of webbing. The olfactory tracts and striae, as well as the anterior pillars of the fornix and the septum pellucidum, were absent. Except at the region of the splenium, the corpus callosum was not represented in its normal form. The microscopic structure of the hippocampal cortex and the dentate gyri was normal.

DRAYER, Philadelphia.

Physiology and Biochemistry

THE CHOLINE ESTERASE CONTENT OF THE CHOROID PLEXUS AND CILIARY PROCESSES. H. HERRMANN and J. S. FRIEDENWALD, Bull. Johns Hopkins Hosp. **70**:14 (Jan.) 1942.

Material was obtained from cattle and pigs and analyzed within one hour of the slaughtering of the animals. The separation of epithelium from stroma, a tedious process, was accomplished by agitating the tissue in saturated solution of sodium sulfate. In the case of the ciliary body much patience is required to keep all the small fragments together when the flakes of epithelium liberated by shaking are poured off with the supernatant fluid. Furthermore, the epithelium of the ciliary processes sticks to the stroma more tenaciously than does that of the choroid plexus. Nevertheless, a stroma fraction poor in epithelial cells and an epithelial fraction very poor in stroma elements can be obtained. From histologic studies the authors estimated the mutual contamination of the two tissues as less than 15 per cent.

Studies of samples of choroid plexus and ciliary processes from animals of the same species gave reasonably consistent results. Choline esterase activity, expressed in cubic millimeters of carbon dioxide, produced in twenty minutes at a temperature of 38 C., corrected for nonenzymatic breakdown, was as follows: (*a*) ciliary body, total activity 250 to 280 cu. mm. in the pig; (*b*) choroid plexus, total activity 169 to 178 cu. mm. in the pig. Both organs in cattle showed only 20 to 25 per cent of the activity of the same tissues in pigs. Compared with Glick's results, the ciliary processes and the choroid plexus fall into the group of tissues with medium esterase activity, being approximately as active as the intestinal mucosa.

The choroid plexus and the processes of the ciliary body show a moderate and similar choline esterase activity, though there is no evidence that the secretory activity of either organ is cholinergic, as compared with that of the epithelium.

PRICE, Philadelphia.

CORTICAL FREQUENCY SPECTRA OF HEALTHY ADULTS. FREDERIC A. GIBBS, J. Nerv. & Ment. Dis. **95**:417 (April) 1942.

Using the Grass method for transferring the electroencephalogram into a spectrum, Gibbs has analyzed over 2,000 spectrums, and believes that it is now possible to ascribe significance to similarities and differences and to speak of the general characteristics of cortical spectrums. This report discusses spectrums from eight cortical areas of 20 normal adults. The results were analyzed by averaging the spectrums from a given area.

"There tend to be gradients in the amount of energy at a given frequency from area to area and from side to side, and also gradients in peak-frequency from area to area and from side to side. These gradients do not all follow a single

plan but differ for different frequency bands. In general, the area which tends to have the fastest peak-frequency also tends to have the highest peak.

"Certain cortical fields tend to beat with a particular frequency but a very similar rhythmic activity is common to the whole cortex, and any area can beat with the same rhythm as any other area. Because of a more energetic, more constant and slightly faster beat, one area may act as a pacemaker for a given range of frequencies. The cortical localization of such pacemakers is not fixed and their behaviour is not constant. They must be described in terms of general tendencies with due regard to differences between the two hemispheres."

CHODOFF, Washington.

IMPERCEPTION FOR THE POSITION OF THE EYELIDS ON ONE SIDE. L. H. RUBINSTEIN, J. Neurol. & Psychiat. **4**:191 (July-Oct.) 1941.

Imperception, or unawareness, of hemiplegia and a feeling of absence of the limbs are closely related symptoms included under the designation of anosognosia. This is fundamentally a disorder of the body schema and depends on an organic cerebral lesion, although similar results may be produced by psychogenic processes of repression and amnesia. There is a fundamental difference between anosognosia and hemiplegia with a fantom limb. The latter is not a disorder of the body schema and depends on loss of sensation, whereas in anosognosia anesthesia may occur but is not essential. Imperception of paresis of the eyelids is part of the syndrome of anosognosia. Rubinstein reports 4 cases illustrating this symptom, in all of which there was left hemiplegia with involvement of the orbicularis oculi muscles and the patient was unaware of whether the left eye was open or shut. In spite of the fact that the patients were not blind, they denied their ability to see a condition which is analogous to the feeling of absence of limbs in the case of imperception of hemiplegia. The symptom was independent of the state of cutaneous and deep sensation; hemianopia and conjugate deviation of the eyes played no role in the mechanism of the disorder, and there were no fantom sensations or motor illusions. In 1 case the imperception was delusionally elaborated, and this is to be regarded as a secondary manifestation. Thus, imperception for the position of the eyelids is part of a general disorder of the body schema. It may, however, be the only sign of imperception, in view of the fact that it is less firmly represented in the schema than are postural and kinesthetic impressions. As to localization, disturbance in body schema may be attributed to parietal lesions, its representations being contralateral and not dependent on the dominant hemisphere. In the majority of cases the condition seemed to be due to a right-sided lesion, which may be attributed to the fact that the schema of the left half of the body is less well established than that of the right. This does not apply to the eyelids, the movements of which are bilaterally symmetric. Since lesions of the right parietal lobe are clinically difficult to localize, this symptom may be of diagnostic aid.

N. MALAMUD, Ann Arbor, Mich.

THE ACOUSTIC AREA OF THE MONKEY (MACACA MULATTA). HARLOW W. ADES and RICHARD FELDER, J. Neurophysiol. **5**:49, 1942.

Cortical responses in the superior temporal gyrus of the monkey to the stimulus of a sharp click were amplified and then recorded oscillographically. Portions of the inferior frontal and temporal lobes were removed to give access to the area studied, and recordings were made systematically at short intervals until the responsive part of the gyrus had been outlined.

Maximum responses always occurred in the angle formed by the junction of the posterior and the medial surface of the superior temporal gyrus. The magnitude of responses diminished somewhat as the distance of the electrode was

increased from this point. The border of the responsive area was sharply demarcated by disappearance of responses in a narrow zone.

The authors show maps of the responsive areas in 7 animals (3 were studied bilaterally). The areas were similar in the different animals. In all cases they were less extensive than was to have been expected on the basis of the anatomic studies by Poliak.

DRAYER, Philadelphia.

EXCITATION AND INHIBITION OF PHRENIC MOTOR NEURONS. ROBERT F. PITTS, J. Neurophysiol. **5**:75, 1942.

Pitts studied the responses to the electrical stimulation of the respiratory centers in cats by recording the changes in potential on a small strand dissected away from the third cervical root of the phrenic nerve. Both the frequency and the intensity of the stimuli were varied.

Stimuli of low intensity or low frequency simulated the normal chemical activation of the respiratory center by producing increased frequency of discharge, increased duration of activity and recruitment of inactive neurons. Similar stimuli to the expiratory center produced exactly the opposite results. Rich synaptic interconnections between the corresponding centers on the two sides were indicated by the fact that stimulation at similar levels in the centers generally produced comparable results, regardless of whether the center stimulated was ipsilateral or contralateral to the fibers being observed. These interconnections permit synchronization with respect to the different phases of respiration. It is thought that normally respiration is augmented by activating more afferent connections to each phrenic neuron and by increasing the frequency of stimuli from the inspiratory centers.

DRAYER, Philadelphia.

THE RELATIVE EFFECTS OF TOXIC DOSES OF ALCOHOL ON FETAL, NEWBORN AND ADULT RATS. ANNETTE CHESLER, GILES C. LABELLE and HAROLD E. HIMWICH, Quart. J. Stud. on Alcohol **3**:1, 1942.

Rats were given intraperitoneal injections of alcohol in doses proportional to the weight of each animal. The effects on fetal rats were obtained by injections into the mother. Newborn rats tended to survive higher doses than either fetal animals or adults. The results are in accord with previous work demonstrating a greater resistance to anoxia in the newborn. The authors suggest that the higher metabolic rate of the brains of adults renders them more susceptible to fatal damage by anoxia and alcohol. Oxygen tension in the blood of the fetus is less than in the blood of the mother. Diminished respiratory activity by the mother under the influence of alcohol diminishes the tension further and may explain the greater susceptibility of fetal animals.

DRAYER, Philadelphia.

THE INFLUENCE OF ALCOHOL ON THE CIRCULATION. ARTHUR GROLLMAN, Quart. J. Stud. on Alcohol **3**:5, 1942.

Grollman analyzes the available experimental results and concludes that the effects of alcohol on the circulation are minor, and probably secondary. Apparent cardiac stimulation is attributed to reflex stimulation from irritation of the gastrointestinal mucosa. The mildly narcotic action tends to allay anxiety. As a result, some benefit may accrue to the circulation secondarily. On the other hand, the cardiac damage formerly ascribed to alcohol is now believed to arise from the relative or absolute thiamine deficiency characteristic of chronic alcoholism. "Beer drinker's heart" is assumed to be related more properly to the amount of fluid ingested than to the alcohol contained in the beverage.

DRAYER, Philadelphia.

Neuropathology

A Congenital Form of Amaurotic Family Idiocy. R. M. Norman and N. Wood, J. Neurol. & Psychiat. **4**:175 (July-Oct.) 1941.

Norman and Wood report an unusual form of lipoidosis in an 18 day old female infant. The family history was inconclusive. The pregnancy and labor were normal, but a few days after birth the baby became "blue" and began regurgitating fluids immediately after feeding; she later died of bilateral renal hemorrhages. The essential postmortem observation was a microcephalic brain, weighing 87 Gm., with pachygyric convolutions and shallow sulci and a particularly small cerebellum. Histologically, the changes were characteristic of amaurotic family idiocy, consisting of widespread swelling of nerve cells and gliocytes, which were distended with lipoid deposits. There was also microscopic evidence of lipoid storage in the reticuloendothelial system of the spleen, lymph nodes, liver and adrenal glands. Besides the fetal time of onset and the extreme micrencephaly, the following histochemical features distinguish the condition in this case from Tay-Sachs disease: (*a*) The occurrence within the cerebral cortex and the Purkinje layer of the cerebellum of large, bizarre, spherical cells, occasionally binucleated and laden with lipoids. These cells resembled atypical neurons, their modified structure probably being conditioned by the fetal onset of the lipoidosis. (*b*) Insolubility of the lipoid material in xylene or boiling chloroform, the substance thus chemically resembling the lipochrome material found in the juvenile form rather than the prelipoids of Tay-Sachs disease. There was also absence of neutral fat, which is common in the latter disorder. (*c*) A heavy crystalline deposit of cholesterol esters throughout the white matter of the cerebrum and cerebellum. In addition, there were an unusually noticeable arrest in myelination and lack of production of fibrillary gliosis. This probably coincides with the fetal onset of the condition and thus may account for the extreme micrencephaly. The atrophy of the cerebellum is not uncommon in cases of lipoidosis, but the atrophy of the olives is unusual. Because of these differences from typical Tay-Sachs disease, the authors regard the condition as an independent form of the disturbance, and although there was no suggestion in the family history of the genetic origin of the disorder, they feel justified in designating it as "congenital amaurotic family idiocy."

N. Malamud, Ann Arbor, Mich.

Post-Traumatic Cerebral Thrombosis and Infarction. J. Arnold deVeer and Jefferson Browder, J. Neuropath. & Exper. Neurol. **1**:24 (Jan.) 1942.

DeVeer and Browder report a case of thrombosis of the right middle cerebral artery which they consider the result of recent cranial trauma, and suggest that the histologic observations may throw light on the problem of delayed posttraumatic cerebral hemorrhage.

A 42 year old steel worker fell 20 feet (6 meters), striking his head, and remained unconscious for twenty minutes. After twelve hours of relative lucidity, left hemiplegia gradually developed, and he became stuporous. Examination revealed bogginess of the scalp over the right parietal region, a pulse rate of 66 per minute and a blood pressure of 170 systolic and 110 diastolic. A roentgenogram of the spine showed a fracture through the left lamina of the second cervical vertebra. A ventriculogram revealed that the ventricular system was small and displaced to the left, with absence of filling of the temporal horn of the right lateral ventricle. A right subtemporal decompression uncovered an intact, though soft, cerebral cortex of a yellowish tint. Exploration of the right temporal lobe failed to disclose a clot. The patient died fifty-seven hours after the injury.

Postmortem examination revealed no evidences of trauma in the bones of the base of the skull or in the dura lining the cranial fossae. The right cerebral hemisphere was larger and softer than the left. The right internal carotid artery and its middle cerebral branch were thrombosed, and a large area of advanced

softening involved the entire region supplied by the right lenticulostriate artery. On microscopic examination, a segment of the right middle cerebral artery adjacent to the mouth of a small branch, showed "separation of the intima, including the internal elastic lamina, from the media of the artery. At certain levels, fragments of media were found adherent to the outer surface of the torn and detached lamina. Frayed and ragged, blood-stained media bordered the area denuded of intima and even streamed into the thrombus that filled the lumen. At one level the tear extended almost through the media, only a few fibers remaining between the lumen and the loose adventitial tissue. The internal elastic lamina, at that plane, showed two rents and there was wide separation of the torn edges."

The authors consider this a case of thrombosis of the right middle cerebral artery induced by traumatic laceration of its inner coats. They suggest three possible results of such a lesion: thrombosis, as in the case described, aneurysm, with delayed rupture, and immediate hemorrhage, due to initial, complete laceration of the vessel walls produced by cranial trauma.

CAMPBELL, Philadelphia.

BRAIN ABSCESS DUE TO ENTAMEBA HISTOLYTICA. AARON STEIN and AVRAAM KAZAN, J. Neuropath. & Exper. Neurol. **1**:32 (Jan.) 1942.

Stein and Kazan review the occurrence of brain abscess due to Entameba histolytica and report a case, which is the sixtieth to be recorded in the literature. Brain abscess is found in about 1 per cent of all cases of amebiasis in which autopsy is performed. In almost every instance there is also an abscess in the liver and/or the lung. This case is of special interest because it shows involvement of the brain without abscess formation in either the lungs or the liver and is the fourth such case to be recorded in the literature.

The patient was a 42 year old man admitted to the hospital in stupor, with a temperature of 102.6 F. He had had watery diarrhea for four years preceding his illness and had lost 50 pounds (22.7 Kg.). Three weeks before admission he had a generalized convulsion, after which he complained of weakness and constant frontal headache. Signs of involvement of the frontal lobes developed, and he lapsed into deepening stupor during the two days before admission. Sigmoidoscopic examination revealed diffuse ulceration of the mucosa, similar to that seen in amebic or bacillary dysentery. Neurologic examination pointed to multiple metastatic abscesses in the brain, with the most marked damage in the left frontal lobe. The cerebrospinal fluid was turbid, under an initial pressure of 240 mm. of water, and contained from 3,000 to 6,000 cells, of which 68 per cent were polymorphonuclear leukocytes, 20 per cent lymphocytes and 12 per cent large monocytes. Of special interest in Gram stains of spinal fluid sediment were large cells with pyknotic nuclei and enclosures of red and white blood corpuscles, the identity of which was not realized until after autopsy. The total protein ranged from 84 to 103 mg. per hundred cubic centimeters. When meningeal signs developed twelve days before death, the sugar in the spinal fluid fell from 55 to 30 mg. per hundred cubic centimeters and the chlorides from 770 to 690 mg. per hundred cubic centimeters.

Gross examination of the brain disclosed a rather large, chronic abscess of the left frontal lobe, which had ruptured into the subarachnoid space. Microscopic examination revealed a few amebas in this area of necrotic material and in its thick, granulomatous capsule. More numerous amebas were seen in small areas of early necrosis in the leptomeninges and in the cerebrum at some distance from the main abscess. The large bowel showed chronic ulceration from the anus to the ileocecal valve. On microscopic examination, amebas were found throughout all layers of the wall of the large bowel, as well as in its lymphatics and blood vessels.

The authors believe that metastasis of the amebas from the large bowel via the vertebral veins seems the most likely explanation for the presence of this abscess of the brain without infection of the liver or lungs.

CAMPBELL, Philadelphia.

POST TRAUMATIC (CONCUSSION) CHANGES IN THE SPINAL CORD, ROOTS AND THE PERIPHERAL NERVES. MARK SCHEINKER, J. Neuropath. & Exper. Neurol. **1**:181 (April) 1942.

Scheinker records a case which he considers one of spinal concussion, with histologic changes in the spinal cord, roots and peripheral nerves. This study is offered in support of the assumption that in cases of spinal concussion there occurs a mechanical lesion of the spinal roots, leading, on the one hand, to contiguous degeneration of the peripheral nerves and, on the other, to retrograde degeneration of the anterior horn cells.

The patient was a healthy, 51 year old man who had fallen violently on his back. Two days later he began to shown signs of involvement of the spinal roots and peripheral nerves of the upper extremities. During the two and one-half months from onset of symptoms until death, there were progressively advancing atrophy and paresis of the musculature of both shoulder girdles and the proximal portions of all extremities, with weakness of both legs, and complete loss of all deep reflexes. Fasciculations were noted in the left arm. In addition to root pains, he had paresthesias and slight disturbances in pain, temperature and touch sensations. Bilateral diaphragmatic paralysis occurred two weeks before death, which was due to bulbar palsy.

The pathologic process consisted of edema, swelling and degeneration of the anterior nerve roots; patchy degeneration of myelin; fragmentation of the axis-cylinders of the peripheral nerves; sievelike rarefaction of the marginal zone of the spinal cord; acute changes in the anterior horn cells, and venous stasis, most evident in the gray matter of the cord, the nerve roots and some of the peripheral nerves. These pathologic changes suggest that the spinal roots were the first to be affected by the damaging factor and that, since the entire periphery of the cord was greatly altered, the effect of the spinal concussion was at play in the area between the margins of the cord and its membranes. The author likens the histopathologic changes in his case to those obtained in Ferraro's experiments. Accordingly, he thinks that there was a direct causal connection between the spinal concussion and the severe changes in the peripheral nerve structures in his case. He believes it possible that these changes were due to a wave of spinal fluid which, originating at the seat of the concussion, acted locally against the spinal cord and was subsequently transmitted along the cord above and below the area of percussion, thus causing marginal degeneration. CAMPBELL, Philadelphia.

PATHOLOGIC CHANGES IN BRAINS OF EPILEPTIC PERSONS WHO DIED DURING STATUS EPILEPTICUS. OSORIO CESAR, Arq. Serv. assist. psicop. estad. São Paulo **6**:243 (Sept.-Dec.) 1941.

The brains of 3 young epileptic persons (15, 17 and 18 years of age) who died during status epilepticus were examined. There was no evidence of intercurrent disease in any of them. The most significant observation in all the brains was the presence of many rounded cavities of varying size throughout the cortex. These cavities were not surrounded by inflammatory changes or glial proliferation. Occasionally ganglion cells near the edges of these cystlike structures seemed to be thinned out, as though compressed. Here and there widely dilated perivascular spaces were seen. Acute, and more rarely chronic, degenerative changes of ganglion cells were noted, with various stages of chromatolysis and alteration in the Nissl substance. Spotty areas of *Ausfall* of cells were seen, with some disorganization of the architectonics of the cortex.

The cases reported are particularly significant because the patients were all young and died in status epilepticus, without evidence of concomitant disease. The author considers the disseminated cortical lacunas of diagnostic significance. The observations confirm the previous observations of Pupo. The anatomic changes indicate the existence of a disturbance of water regulation in the brain—an intracerebral hydrops. SAVITSKY, New York.

CHANGES IN THE SPINAL CORD IN LANDRY'S PARALYSIS. E. MOSIG, Ztschr. f. d. ges. Neurol. u. Psychiat. **170**:331 (Sept.) 1940.

Mosig reports 4 cases of Landry's paralysis, with studies of the spinal cord and nerve roots. Two of the patients were males and 2 females. The ages varied from 1 to 58 years. The duration of the illness was up to ten days. The clinical picture in each case was that of ascending paralysis. In none of the cases was there any evidence of inflammatory disease in the spinal cord. In fact, no significant alterations were noted in any of the structures of the cord. The ganglion cells were intact. There were severe changes in the nerve roots, especially the anterior. These lesions were apparently degenerative, involving especially the axis-cylinders. There were less striking alterations in the myelin sheaths.

SAVITSKY, New York.

Psychiatry and Psychopathology

THE HEREDOCONSTITUTIONAL MECHANISMS OF PREDISPOSITION AND RESISTANCE TO SCHIZOPHRENIA. FRANZ J. KALLMANN and S. EUGENE BARRERA, Am. J. Psychiat. **98**:544 (Jan.) 1942.

The difficulties in arriving at a somatogenic concept of schizophrenia based on heredoconstitutional mechanisms are indicated by Kallmann and Barrera. The authors assume that the predisposition to schizophrenia is based on a single genetic factor which is specifically autosomal and recessive, but not always fully expressive. The assumption is substantiated by statistical studies on twins and kinships. These studies demonstrate that children of a schizophrenic parent have nineteen times the average probability of acquiring the disease. The expectancy for homozygous twins is 70 to 80 per cent. The susceptibility is autosexual, since there is no significant sex difference. The specificity is indicated by an increase only in mental disorders of the schizophrenic type. Recessiveness is demonstrated in consanguinity. In studying the factors of resistance to schizophrenia, Kallmann and Barrera find that in the majority of cases in which only one twin has schizophrenia the other is physically stronger. Furthermore, in cases other than those of twins, the tendency toward extreme deterioration corresponds to a high asthenic and a low athletic component of habitus, according to the Sheldon technic. This, the authors feel, indicates that the athletic component is a factor of resistance to the development of schizophrenia.

FORSTER, Boston.

ANALYSIS OF THE MENTAL DEFECT IN CHRONIC KORSAKOV'S PSYCHOSIS BY MEANS OF THE CONDITIONED REFLEX METHOD. W. HORSLEY GANTT and WENDELL MUNCIE, Bull. Johns Hopkins Hosp. **79**:467 (June) 1942.

The pavlovian method of conditioned reflexes was placed in clinical use and the results formulated in terms compatible with psychiatric orientation in 3 cases of the Korsakov psychosis. Essentially the method consisted in exposing the patient to a simple and orderly series of events chronologically arranged and within the grasp of his sensorium. Spontaneous active participation and collaboration were reenforced by a desire to avoid pain.

The patients were tested for their ability to react defensively in anticipation of an unpleasant stimulus: namely, to wink defensively to an anticipated tap at the base of the nose, or to withdraw the hand from an electrode plate in anticipation of a faradic shock. Similar results were obtained with both methods and give experimental proof of the following characteristics of the psychosis: (1) retention deficit, the span being sometimes very short; (2) poor memory for learned material; (3) special difficulty in recognition of values of separate items of the test, when each item could be named; (4) the importance of the verbal formulation for the determination of the *Einstellung;* (5) complete inability to analyze and synthesize when the patient was left to the spontaneous use of the sensorium, unaided by

verbalization; (6) motor and verbal formulation inconsistent one with another, indicating probable thinking disorder, in the failure to exclude paradox; (7) failure of new learned responses ever to become "fixed" by repetitions, no matter how numerous, probably because of retention defect, in contrast to the preservation of old responses; (8) ability to carry out direct command, again with the limitation of the retention span.

In conclusion, the patient with the Korsakoff psychosis thus lives on the past perhaps rather than in the past, on a meager fund of what has been salvaged from his more or less remote experiences, while the present, with its demands for new responses, is entirely beyond his horizon.

PRICE, Philadelphia.

FACTORS AFFECTING THE PROGNOSIS OF PARANOID DISORDERS. CHARLES W. MILLER JR., J. Nerv. & Ment. Dis. **95**:580 (May) 1942.

In line with the recent tendency to avoid linking diagnosis and prognosis in cases of such psychiatric disorders as schizophrenia, Miller suggests a similar reevaluation of the paranoid conditions. Using as material a previous study in which a large number of patients with reversible psychoses with paranoid features proved to make a good recovery, he attempts an analysis of the factors common to the recovered patients.

The presence of any or all the characteristics which go to make up the classic prepsychotic paranoid personality was associated uniformly with a poor prognosis, while, conversely, a sudden onset of the paranoid picture as an abrupt departure from the usual personality was associated with a high recovery rate. More recoveries occurred in the middle age group and fewer at either end of the age scale. Fixed delusions were of bad, and shifting ones of good, prognostic import, while grandiose ideas almost invariably indicated a poor outlook. Environmental confirmation of the delusional system was not a determining factor in the outcome of the cases. Definite precipitating causes were rare, but when they existed were more often than not associated with a favorable prognosis. In patients who had been happily married, there were 50 per cent more recoveries than in the large number of those who had experienced marital incompatibility. Those patients whose overt behavior took a socially acceptable form were more often returned to the community than were those who resorted to violence, threats or alcohol, but this did not necessarily indicate a more complete recovery. The presence of insight bore little constant relation to the outcome in the case, while the gaining of intimate rapport with the physician often proved destructive. The assets of the individual patient were the most important factor and, if strong enough, were often able to overcome many indicators of a bad prognosis.

CHODOFF, Langley Field, Va.

PSYCHOTIC MANIFESTATIONS IN CHRONIC ENCEPHALITIS. JULIUS L. NELSON and JOSEPH ZIMMERMAN, J. Nerv. & Ment. Dis. **95**:589 (May) 1942.

On the basis of 30 cases, Nelson and Zimmerman made an analysis of psychoses associated with epidemic encephalitis. In all cases there was some degree of mental and physical impairment. In 20 cases the reason for admission to the hospital was excitement and assaultive behavior, while depression with suicidal attempts accounted for admission in 5 instances. Abnormal prepsychotic personalities, indifferent or unsympathetic families, occurrence of the illness early in life and a greater degree of physical handicap were factors which appeared to be important in the uncovering of the psychotic reactions. These were usually not clearcut types and resembled only superficially the well defined psychotic syndromes. Situational factors and real frustrations played a major role, especially in the depressions. The schizophrenia-like features, such as paranoid trends and hallucinations, were usually of short duration and were directed toward members of the patient's family. Emotional instability was common to all the cases. The

authors believe that the peculiar nature of the handicap faced by the encephalitic patient, being both physical and mental, does not allow him to transfer his activities satisfactorily from one field to another. Since his difficulty is progressive, he must constantly lower his level of adjustment. Irritability and emotional instability result, and, depending on his personality makeup, the patient then becomes depressed, assaultive, paranoid or delinquent.

CHODOFF, Langley Field, Va.

INEBRIETY: A CLASSIFICATION. IRA A. DARLING, Quart. J. Stud. on Alcohol **2**:677, 1942.

Darling reports 11 cases representing the following types of inebriety: (1) those associated with a frank psychoneurosis or psychosis; (2) those associated with organic lesions of the brain; (3) those associated with mental deficiency; (4) those associated with an effort at escape from a painful life situation fully or partially recognized as such by the patient; (5) those associated with an effort at escape from a painful life situation not recognized as such by the patient, and (6) those associated with habit formation through frequent repetition, social custom and "physiologic craving."

Alcohol is used as a psychologic "crutch" in all but the last type. Here there seems to be no underlying maladjustment, and the prognosis after treatment is considered good.

DRAYER, Philadelphia.

THE ALCOHOLIC PERSONALITY: A STATISTICAL STUDY. NATHAN MOROS, Quart. J. Stud. on Alcohol **3**:45, 1942.

Moros classified on the basis of race all World War veterans admitted to the United States Veterans Administration Facility, Northport, L. I., between Jan. 1, 1936 and Jan. 1, 1939. Four of these groups were large enough to permit comparisons. Chronic alcoholism was found to be prevalent among members of two of the groups and not among those of the other two. The frequency of psychoneurosis was found to be highest in the nondrinking groups. Moros asserts, however, that there may have been many unrecognized psychoneurotic persons among those classified as having uncomplicated alcoholism. The author concludes that "the label of chronic alcoholism as a primary mental diagnosis appears to be rarely justified. A close study of alcoholics would probably lead to the recognition of a basic personality defect preceding the alcoholic habit."

DRAYER, Philadelphia.

A STUDY OF WAR ATTITUDES. P. E. VERNON, Brit. J. M. Psychol. **19**:27, 1942.

One hundred and fifty men and 80 women of diverse outlooks and of various economic and educational levels answered a questionnaire dealing with war attitudes, opinions, activities and background data. The responses were classified into five groups which were labeled: cheerfulness-complacency; wishful thinking; antisocialism; projective or paranoid opinions, and moralistic opinions. Scores on these tests were intercorrelated with sex, age, war work, hardships, etc. The type of person designated as a "good citizen" showed several activities desirable in civilians in wartime, and those in this category tended toward moralistic and projective opinions. Various other groups, such as conscientious gas mask carriers, showed distinctive trends of opinion. Persons who had undergone much bombing were rational, liberal and less favorable to official viewpoints, but scored high in good citizenship activities. Those suffering other wartime hardships also showed negative attitudes, but were below average in war activities, interest and knowledge. Persons who were well educated and highly informed about the war were rational, critical and socialistic in their views, and often quite negative; yet they were close to average in their war work, savings and air raid precautions. This shows that knowledge and consequent rational and critical attitudes do not necessarily inhibit helpful activity.

Vernon discusses the theoretic implications of attitudes as demonstrated in this analysis—for example, the potency of intellectual experience, both general educational background and knowledge about involved issues, as an influence on attitudes. Though there is a close relation between verbal attitudes and behavior, it cannot be said that unfavorable attitudes are always accompanied by appropriate behavior, since the influence of other factors, both emotional and intellectual, is ever present.

ALLEN, Philadelphia.

RATIONALE OF CONVULSION THERAPY. D. W. ABSE, Brit. J. M. Psychol. **19**:262, 1942.

Abse believes it is important to approach the problem of convulsion therapy from a psychologic viewpoint since psychologic alterations are so obvious and striking, although he does not ignore the possible value of physiologic studies.

Anxiety is inextricably bound up with convulsion therapy, as the patient is repeatedly exposed to danger situations. The fear, which is recognized to have important dynamic value in many situations, results in repression. Since, for example, schizophrenia may be termed the disease of unsuccessful repression, the induction of repression may be assigned an important role in the dynamics of this treatment. In addition, during the convulsion, the physiologic conditions of birth are reestablished, which would make it seem a forceful affective symbol. Since repression is not the most desirable method for establishing a new balance in the psyche and may be responsible for the evidence of personality deterioration following convulsion, this form of therapy is contraindicated in cases in which some type of analytic therapy is possible.

In depressive states, already accompanied by massive repression, this rationale may still hold true, for the repression is enabled to occur at a more efficient level. Though a transference situation is often built up during the process of treatment, concomitant psychotherapy is best limited. The prognosis depends on the extent and fixity of the regression.

ALLEN, Philadelphia.

Diseases of the Brain

NEUROLOGICAL ASPECTS OF SIMPLE MASTOIDITIS. E. H. TROWBRIDGE JR., J. Nerv. & Ment. Dis. **95**:575 (May) 1942.

Trowbridge studied a series of 112 patients, each with a diagnosis of simple mastoiditis, for the incidence of neurologic signs, such as headache, nausea and vomiting, fundal changes, nystagmus, reflex alterations and changes in cranial nerves. In contrast to the observations of Neilsen and Courville on a comparable series, in only a few patients were positive neurologic signs found. Abnormalities in the spinal fluid were also uncommon.

CHODOFF, Langley Field, Va.

THE OCCURRENCE OF POLYNEURITIS AND ABNORMAL PUPILLARY REACTIONS IN CHRONIC ALCOHOLISM. LAZARUS SECUNDA and ELLSWORTH H. TROWBRIDGE JR., Quart. J. Stud. on Alcohol **2**:669, 1942.

Secunda and Trowbridge studied the records of 641 patients with chronic alcoholism. All in the series had negative Wassermann reactions of the cerebrospinal fluid. Seventeen per cent had polyneuritis and 44 per cent had anomalous pupils. The highest incidence of both abnormalities was in the group of patients with alcoholic psychoses.

DRAYER, Philadelphia.

ALCOHOLISM AND CRIME. RALPH S. BANAY, Quart. J. Stud. on Alcohol **2**:686, 1942.

Banay made an extensive survey of the 3,135 admissions to Sing Sing prison during a two year period (1938 to 1940). The group of delinquents in which alcoholism had led to the commission of crime was analyzed. The remainder,

including persons whose use of alcohol was only incidental in their criminal careers, were used as controls.

In 25 per cent of the total number, alcoholism was closely related to the commission of the crime or was directly responsible for it. The alcoholic group was characterized by a greater tendency toward assaultive and violent crimes. In the general group, crimes against property predominated. Evidence of psychopathology was more easily found in the alcoholic criminal than in the average offender, but the author points out that little effort is being made to take therapeutic advantage of this fact. Proper institutions for the rehabilitation of these persons are recommended.

DRAYER, Philadelphia.

DISTURBANCE OF DRIVE IN A CASE OF MENINGIOMA ARISING FROM THE LOWER BORDER OF THE FALX. KURT BERINGER, Ztschr. f. d. ges. Neurol. u. Psychiat. **171**:451 (March) 1941.

Beringer reports the case of a large frontal tumor without signs of increased intracranial pressure occurring in a clergyman, aged 31. Unusually detailed information about mental content and processes could be obtained from this cooperative and intelligent patient, who was not torpid and showed no striking signs of intellectual enfeeblement or retardation. Because of the war emergency, experimental psychologic studies were not feasible.

The patient was admitted on May 5, 1940. His wife stated that she had observed increasingly severe mental changes for five months. The presenting symptom in retrospect, however, dated back to four years before admission, when he had a convulsive seizure during the night. On three occasions, during September 1939, October 1939 and January 1940, he suddenly had an urge to move his bowels, and on two occasions was incontinent of feces. Soon after January 1940, his sermons were not as original, colorful or well organized as they had been. At the same time he began to lose interest in current events and even in what was going on in his own community. He became neglectful of his pastoral duties and lost interest in finishing various things which were left undone. When these were called to his attention, he looked after them for a time but again forgot them. On one occasion he forgot to attend a funeral. Such lapses of memory were, however, rare. When he did perform his duties he seemed to do so correctly. He lay in bed in the morning instead of attending services. His wife had to prod him. There seemed to be absence of appropriate effect, but no depression. He was unconcerned when he missed appointments or made other mistakes. He lay down often during the day. During February and March he began to leave even simple things unfinished. When shaving or playing the piano he would suddenly stop and stare, doing nothing, and then continue when reminded of what he was doing. At times he failed to take food placed before him. Sometimes he would come in incompletely dressed when visitors were present. He became somewhat erethitic sexually. As time went on he failed completely to prepare his sermons. There was never any evidence of pronounced dementia. He would answer questions promptly and relevantly, but when not addressed he usually remained quiet. He made no effort to start or continue a conversation. He was finally brought to the hospital because he lay in bed up to 11 a. m., made no effort to eat and wandered around aimlessly, going back to bed at 4 p. m.

Objective examination showed slight deviation of the tongue to the left, defective swinging of the right upper extremity while walking and occasional urinary incontinence. Roentgenograms of the skull were without significance. The pineal gland was not displaced. The total protein of the spinal fluid was 34.8 mg. per hundred cubic centimeters. Pneumoencephalograms showed pushing down of the anterior part of the lateral ventricles, especially on the left side. Electroencephalograms showed atypical slow waves anteriorly, with definite phase reversal in the right precentral region. Atypical delta waves were seen in the left prefrontal region.

The patient preferred to lie in bed with eyes closed or looking blankly ahead of him; he showed no desire to occupy himself. He was mildly euphoric. He occasionally has compulsive sexual thoughts, especially when alone, but showed no regret or shame about such thoughts and stated that he could not help their appearance. There were usually no spontaneous thoughts or free associations; even external stimuli did not quicken his thought processes or associations; his apperceptive background was not used to react to new experiences. There was marked poverty of mental content. He showed some interest in his family but none in ward routine, his profession or politics. He did not tell of any plans for the future. He would often stop eating during a meal and go to bed; he often had to be prodded to finish dressing. He was not negativistic or uncooperative; he was just blocked. In spite of his idleness, he did not feel that time was dragging. Lack of spontaneity seemed somewhat less in the evening. He acted almost normally when strangers were around; he appeared alert and apparently interested; he answered promptly and showed no evidence of enfeeblement.

An operation was performed on May 24. Through a left transfrontal approach, a large subfrontal tumor was exposed, which extended under the falx to the opposite side. The tumor, a meningioma, which weighed 125 Gm., was removed in toto. After the operation he regained some interest in things, and his affect became somewhat more adequate. The lack of drive and spontaneity persisted.

The lack of drive is emphasized as the dominant feature in the clinical picture. It was a disorder of the will and of the whole personality. No definite attempts at anatomicoclinical correlation are attempted except to note that this type of clinical complex is more likely to take place with bilateral lesions of the frontal lobe.

SAVITSKY, New York.

Treatment, Neurosurgery

ELECTROSHOCK TREATMENT IN THE PSYCHOSES. L. H. SMITH, J. HUGHES, D. W. HASTINGS and B. J. ALPERS, Am. J. Psychiat. **98**:558 (Jan.) 1942.

Smith, Hughes, Hastings and Alpers discuss the contraindications, technic, complications, selection of cases and results of electric shock therapy of the psychoses. Patients with definite organic disease are not subjected to the treatment. In the event of osteoarthritis of the spine curare is used. The authors use an alternating current of 200 to 400 milliamperes at 80 to 175 volts flowing from one-tenth to six-tenths second. Three types of reaction are possible: (1) brief unconsciousness; (2) more prolonged unconsciousness accompanied by the development of abnormal reflexes, and (3) unconsciousness followed by tonic, then clonic, convulsions. The authors usually administer three treatments, the total number varying from twelve to fourteen. Fractures occurred in 5 per cent of 156 patients. Memory defects were present in almost all patients, but in none were they permanent. No neurologic sequelae have been encountered. Complications were rare and included prolonged apnea, auricular fibrillations and dislocations of the jaw. The authors obtained best results in the treatment of involutional melancholia and long-standing manic-depressive psychoses. They state that the electric shock method is preferable to metrazol therapy, but despite favorable clinical results, they warn against its routine and indiscriminate use.

FORSTER, Boston.

RESULTS IN THE USE OF AMPHETAMINE (BENZEDRINE) SULFATE AS AN ADJUVANT IN THE TREATMENT OF CHRONIC ALCOHOLISM. WILFRED BLOOMBERG, Am. J. Psychiat. **98**:562 (Jan.) 1942.

Bloomberg reports the results of benzedrine therapy in a series of 56 persons with chronic alcoholism. He is careful to point out that benzedrine sulfate is by no means a cure for alcoholism, but rather is an adjunct to other forms of therapy.

The dosage used ranged up to 140 mg. daily. While admitting the defects of a statistical approach, Bloomberg tabulated 22 of his 56 patients as now being total abstainers; in only 19 cases did he obtain poor results. He states that the usefulness of benzedrine sulfate is based on the following results: The drug combats general malaise and depression; hospitalization is avoided; establishment of rapport with the physician is aided; ingestion of a substance is utilized, and mood swings are smoothed out. Bloomberg concludes that benzedrine sulfate is a useful adjunct to any method of treatment of chronic alcoholism. FORSTER, Boston.

SULPHANILAMIDE AND SULPHAPYRIDINE IN EXPERIMENTAL CEREBRAL WOUNDS. E. H. BOTTERELL, E. A. CARMICHAEL and W. V. CONE, J. Neurol. & Psychiat. **4**:163 (July-Oct.) 1941.

When 500 Gm. of sulfanilamide and sulfapyridine crystals was placed in brain defects of 11 and 13 cats, respectively, the former drug disappeared in from eighteen to thirty-six days and the latter in from forty-four to fifty-eight days. In all cases the drug acted as a foreign body, causing a local inflammatory reaction, through which it was encapsulated and ultimately absorbed. In the early stages, the inflammatory reaction consisted of polymorphonuclear leukocytes and phagocytic cells, which invaded the crystals. Later, this was replaced by lymphocytes, plasma cells and giant cells. When absorption was complete, a scar of mixed neuroglia and connective tissue resulted. More polymorphonuclear leukocytes surrounded sulfanilamide in the early stages, and heavier encapsulation with connective tissue occurred about sulfapyridine. Because of its quicker absorption and the shorter period of the inflammatory reaction, sulfanilamide seems to be the drug of choice for local application in cerebral wounds. There were no changes in the nerve tissue at a distance from the drug, the reaction remaining purely local. The local scarring was no more extensive than that following wounds uncomplicated by the use of sulfanilamide or its derivative. The highest level of either drug found in the blood, resulting from absorption from the drug in the cerebral wounds, was not sufficient to be of therapeutic significance. There was no impairment in the general health of the animals and no pathologic changes in the internal organs which could be attributed to the drug. In no instance did postoperative infection occur and the authors are of the opinion that use of sulfanilamide or a derivative is indicated in potentially infected or infected wounds, even though the bacteriostatic and bacteriolytic actions of such drugs have not yet been conclusively proved. However, they advise caution, since the drugs act as foreign bodies and excessive quantities should never be used. Of practical significance is the effect of sulfapyridine crystals in controlling bleeding from smaller venous channels. N. MALAMUD, Ann Arbor, Mich.

Society Transactions

ILLINOIS PSYCHIATRIC SOCIETY

WALTER H. BAER, M.D., *President*

Regular Meeting, March 5, 1942

Adaptation of the Central Nervous System to Varying Concentrations of Alcohol in the Blood. DR. MILTON ROSENBAUM, Cincinnati.

Many authors associate specific concentrations of alcohol in the blood with the state of clinical intoxication, and to some a concentration of 0.15 per cent is synonymous with intoxication. These attitudes persist despite the fact that it has been known for years that the symptoms of alcoholism are more apparent when the alcohol concentration in the blood is rising than when it is falling. It is obvious that if the concentration of alcohol in the blood is the sole factor in the development and maintenance of intoxication, there should be no difference in symptoms during the rising or the falling of the alcohol curve so long as the concentration is the same in each phase.

In a series of experiments with rabbits it was observed that the hepatectomized animal was unable to oxidize alcohol (Mirsky, I. A., and Nelson, N.: The Influence of the Pancreas and the Liver on the Oxidation of Ethyl Alcohol, *Am. J. Physiol.* **127**:308 [Sept.] 1939), and hence the alcohol concentration of the blood remained relatively constant. The concentration could be raised and maintained at any desired level by the intravenous injection of alcohol. When the alcohol level of the blood was raised rapidly (in one to two minutes) to 100 mg. per hundred cubic centimeters nystagmus and incoordination developed, and within five minutes after the injection the animals were in deep coma. However, from ten to thirty minutes after the onset of coma the animals quickly returned to a normal state despite the fact that the alcohol content of the blood had not changed appreciably. These changes could be repeated by the further injection of alcohol until a level was reached (400 mg. per hundred cubic centimeters) at which the animal passed from coma to death. Similar observations were made with normal rabbits. Electroencephalograms of 4 normal rabbits revealed a correlation between the clinical state and the cortical waves. Thus, during coma large slow waves appeared, only to disappear when the clinical state returned to normal, in spite of an unaltered concentration of alcohol in the blood. This suggested that the central nervous system of the rabbit can adjust itself to increasing amounts of alcohol and that a time factor is involved in this adaptation (Mirsky, I. A.; Piker, P.; Rosenbaum, M., and Lederer, H.: "Adaptation" of the Central Nervous System to Varying Concentrations of Alcohol in the Blood, *Quart. J. Stud. on Alcohol* **2**:35 [June] 1941).

Eight persons with chronic alcoholism were given by mouth 1.0 Gm. of ethyl alcohol (30 to 50 per cent solution) per kilogram of body weight after an overnight fast. In from one to two hours after the first dose, 0.25 to 0.5 Gm. of alcohol per kilogram was given to maintain the blood level. An attempt was then made to determine the level at which the patient became obviously "drunk" and the subsequent level at which he became "sober." In all the experiments the patient became intoxicated at a lower level than that at which he became sober. The time for the "sobering-up" process varied from four to ten hours. A typical example was that of a patient who became "drunk" at an alcohol concentration in the blood of 192 mg. per hundred cubic centimeters, and five hours later was sober, with a concentration of 273 mg. per hundred cubic centimeters. Two

patients were given large doses to make them comatose, and then 9 cc. of a 10 per cent solution of metrazol was injected slowly; in a few minutes the patients became conscious and responsive despite the fact that there was no decrease in the concentration of alcohol in the blood. In 1 patient the amount of alcohol in the blood preceding the metrazol was 428 mg., and eleven minutes later, when he was out of coma after administration of metrazol, it was 439 mg. per hundred cubic centimeters. Another patient was given alcohol immediately after recovering from a previous intoxication. During the first episode the subject became intoxicated at a level of 219 mg. per hundred cubic centimeters and was sober eight hours later when the level was 282 mg. The administration of alcohol at this point resulted in intoxication at a level of 304 mg. per hundred cubic centimeters, and three hours later he was sober at a level of 324 mg. per hundred cubic centimeters.

These studies reveal that gross symptoms of intoxication disappear at concentrations of alcohol in the blood which originally were adequate to induce symptoms in the same person. This suggests that the central nervous system of man can compensate to its alcoholic milieu so that resistance to the pharmacologic effect of alcohol is developed after a variable period. The time required for this "adaptation" apparently varies from species to species and from person to person. These findings support the suggestion by Newman that a change in the responsiveness of the nervous system to alcohol, rather than a change in the rate at which alcohol is removed from the tissues, accounts for the tolerance to alcohol. Recently Newman (Newman, H., and Abramson, M.: Relation of Alcohol Concentration to Intoxication, *Proc. Soc. Exper. Biol. & Med.* **48**:509 [Nov.] 1941) confirmed our results, using a delicate psychologic performance test, rather than our gross tests for "drunkenness," for correlation with the level of alcohol.

The possibility suggested by our data and the results of the more recent studies by Newman, namely, that the nerve tissues may function efficiently despite a high concentration of alcohol, casts doubt on the validity of the use of the alcohol concentration in the blood as an index of intoxication. The diagnosis of intoxication should be made on clinical grounds, and the concentration of alcohol in the blood or other body fluids should serve only as an indicator that alcohol has been imbibed and is the probable toxic agent responsible for the clinical condition.

DISCUSSION

Dr. Jules H. Masserman, Chicago: The experimental contributions to this subject by my associates and me—and I presume they furnish the reason for my being asked to discuss this paper—have been relatively minor; nevertheless, our results furnish ancillary evidence in support of Dr. Rosenbaum's conclusions as to the complexity and variability of the effects of alcohol on the central nervous system. In an experimental study reported about two years ago (Masserman, J. H., and Jacobsen, L.: The Effects of Ethyl Alcohol on the Cerebral Cortex and the Hypothalamus of the Cat, Arch. Neurol. & Psychiat. **43**:334-340 [Feb.] 1940), it was shown that concentrations of alcohol greater than 0.06 per cent depress the activity and electrical reactions of the cerebral cortex, but concurrently increase the functions of the hypothalamus in emotional mimetic expression. Thus, cats intoxicated with sufficient alcohol (up to 4 cc. per kilogram) to induce a deep stupor could be aroused readily and made to show reactions of extreme sham rage or fear when the hypothalamus was stimulated with electrical currents even weaker than were necessary before the alcoholic intoxication. In a follow-up study of this interesting phenomenon (Masserman, J. H.: Stimulant Effects of Ethyl Alcohol in Cortico-Hypothalamic Functions, *J. Pharmacol. & Exper. Therap.* **70**:450, 1940), it was shown further that, although the direct injection of ethyl alcohol in concentrations greater than 0.06 per cent produced toxic effects in all portions of the central nervous system, concentrations below 0.01 per cent actually stimulated the emotional mimetic functions of the hypothalamus, whereas the injection of small doses of alcohol intravenously (less than 1 cc. per kilogram) also increased the electrical reactivity of the cortex. In

both studies the curves of intensity and the duration of these effects varied with the rate of injection of the alcohol, the type and depth of the anesthetic and the condition of the animal; moveover, in unanesthetized recovery preparations the results also differed considerably from animal to animal. It was demonstrable, then, that the nature and duration of the total pharmacologic effects of alcohol depend not only on its concentration in the central nervous system but on its different actions on the cortex and the subcortex, on the concurrent influences of other drugs and on various unexplored factors specific to the individual organism. Now that Dr. Rosenbaum and his colleagues have demonstrated the additional factor of the rapid adaptation of the central nervous system even to heavy alcoholic insults, it is difficult to see how it can be maintained any longer that the determination of the amount of alcohol in a single sample of blood from a human subject can furnish any but the roughest indication as to whether the psychobiologic functions of that subject were sufficiently disorganized to fulfil the vague criteria of "intoxication."

Dr. Roy Grinker, Chicago: Alcohol attacks the cerebellar system early, as exemplified by the early-appearing disturbances in equilibrium. Persons with chronic alcoholism acquire a coarse intention, cerebellar tremor. This same tremor may be abolished by extirpation of certain prefrontal areas and, in many cases of chronic encephalitis, by ingestion of alcohol. Thus, in the motor system alcohol first causes a symptom, and then, by acting on another part of the nervous system, abolishes the symptom. May this apply to other parts of the nervous system? Is the decrease of signs of alcoholism due to adaptation or to increased effect, reaching thresholds of other centers?

Dr. Lloyd H. Ziegler, Wauwatosa, Wis.: I am not unmindful of the points which Dr. Grinker has brought out. There is much to be said in behalf of Dr. Rosenbaum's interesting concept. Perhaps some clinical experiences may throw light on the matter. One sees persons who can drink considerable quantities of alcohol during the earlier years of life and still remain rather clear and behave well. In later years a smaller quantity of alcohol will intoxicate them or produce great changes in behavior.

This makes one curious to know what has happened to the nervous system of such a person. This change in tolerance to alcohol comes on as sharply as the need for bifocal lenses, and often at about the same time in life. The capillary beds in the brain may be undergoing changes, as they are in the skin and other organs during the fourth and fifth decades.

Dr. Milton Rosenbaum, Cincinnati: As far as the psychobiologic effect of alcohol is concerned, it is important whether one desires to get drunk or not.

I agree with Dr. Grinker with regard to the beneficial effect of alcohol on the tremor of Parkinson's disease and at times on the tremor due to the previous ingestion of alcohol itself. When alcohol is ingested, the concentration in the blood mirrors the tissue concentration. Therefore the concentration of alcohol is the same in all parts of the brain, from the frontal lobes to the hindbrain. Yet the symptoms of alcoholism are probably due to interference with the normal function of the so-called higher centers, as is the case with most toxins that affect the central nervous system. It probably comes down to the factor of the inherent resistance of the cells in different parts of the brain rather than to the involvement of any one group of cells in a specific fashion. Therefore, it is probable, as Dr. Grinker suggested, that the symptoms in part may be due to certain mechanisms having to do with release of cortical inhibition. However, my studies revealed that brain tissue (perhaps any part) can function efficiently despite a high alcohol concentration in the tissue itself. I have no data as to the mechanism of this "adaptation."

The Critical Moment in Psychotherapy. Dr. Maxwell Gitelson, Chicago.

In somatic medicine the indications for the physician's therapeutic activity stem from his precise understanding of the implications of a syndrome in terms of

anatomy, physiology and pathology. Similarly, in psychologic medicine the indications can, and must, be no less strict. Enough is known of the laws of human experience and behavior to expect the well trained psychiatrist to act definitely in terms of what the patient's problem really is. Failure to do this may be quite as costly to the patient with an acute neurosis or psychosis as an operation on the abdomen when the pathologic process is in the chest. The critical moment in psychotherapy is a complex comprised of the interaction of the psychiatrist's immediate capacity for meeting the patient's particular therapeutic need, based on explicit knowledge sensitively applied, and of the patient's readiness to use help when he actually senses its real availability.

This thesis was demonstrated in the successful psychotherapy of a psychosis in a young married woman who had acquired bizarre and intense persecutory delusions in a setting of discouraging financial struggle toward a career on which her husband was already launched. The history made it possible to infer that the patient had suffered a severe blow to her self esteem on the basis of secret self comparisons with her husband and other young professional men and that this had produced bitter resentment, which this decent person had eliminated from awareness. Instead, her hostility had been turned against herself in the form of the psychotic content.

The first definitive step in treatment was to ignore her administrative status as a clinic patient. She was met in the lobby of the hospital, greeted as a social equal and conducted personally to a private office. The next step was to listen to the story of her psychosis and then to undermine its validity by an immediate approach to the injured pride, saying, for example, "It looks to me as if you are really upset by the things you are having to do (menial work) in the interest of your career. That's hard to bear when you feel that you are the equal of the others who are getting what you feel you also deserve." The patient was free of her psychotic delusions at the next interview, twenty-four hours later. Instead, she was deeply depressed. The fantastic character of her original story had dawned on her in the interim, and she had been able to reconstruct the actual emotional situation in which she had found herself. This was essentially what had been implicit in the bare facts of the history as given by the husband: profound and mounting feelings of depreciation and injured pride.

During two succeeding interviews, at intervals of two days, it was possible to bring into the open the hostile resentment toward those whose lot was easier and thus far more successful than her own. Space does not permit the demonstration here of the technic used to protect her against the evolution of the deepest aspects of her hostility. The effort was successful, and the depression which had followed the psychosis disappeared within a week.

Over a period of three and a half months thereafter the patient was seen five times, and further aspects of her reaction were analyzed. Fifteen months later the patient was still well and was making really successful strides toward her career. The shock treatment which had been advised at another clinic had not been necessary. Instead, the patient had had an opportunity for an integrative experience.

DISCUSSION

DR. S. A. SZUREK, Chicago: It is an often stated truism that the psychiatrist's chief instrument of diagnosis and therapy is his own personality. A capacity to identify with another person and thus comprehend his conflicts while retaining one's freedom to act in relation to him without the crippling and distorting anxiety of overidentification is a characteristic of basic importance in the equipment of the psychotherapeutist. This equipment, though occasionally present to some extent in a person as a result of his ordinary life experience, can be acquired only by suitable training measures which eventuate in gaining insight into and freedom from distorting trends in one's own self organization. When attained, it permits the psychotherapeutist not only to locate with precision the nature of the frustrating interpersonal experiences of the patient, as exemplified

in Dr. Gitelson's case, but to evaluate the degree of the resulting disequilibrium in the patient's personality. The latter ability obviously measures the skill of the psychiatrist.

It is this capacity to estimate the severity of the disorder through direct personal contact with the patient that I wish to discuss. As Dr. Gitelson points out, the skilled diagnostician in all branches of medicine bases his prognostic impression not alone on the presenting symptoms but on all the relevant factors in the situation. The modern clinician seeks to determine the remaining reserve of functional capacity of the affected organ or that of the entire organism rather than to rest content with conclusions based on the severity of symptoms.

Every experienced psychiatrist can give numerous instances from his practice in which the apparently obvious hysterical symptoms were the presenting signs of an incipient, severe schizophrenic psychosis, as well as cases in which the patently paranoid, schizophrenic symptoms denoted an acute reaction of a well integrated personality to specifically overwhelming thwarting and one of good prognosis. In less experienced hands such conditions may lead either to delay of the prompt treatment essential or to an indiscriminate, if not a disguised sadistic, use of minor electrocution of the already tottering and threatened ego of the patient. I cannot forego the opportunity to mention another technic of convenience, or of incompetence, which, though often relatively harmless, may on occasion be severely injurious. I refer to the fostering or encouraging of the regressive tendencies of an acutely disturbed patient who seeks the help of the psychiatrist to maintain his ego supremacy over them. If the anxiety of the physician is sufficient, such a patient may be incarcerated, or at least be sent away from his usual routine, which may complete his surrender to the dissociated trends and either wreak havoc with his future or prolong the disorder. If Dr. Gitelson had not shown to the patient his supreme confidence in her capacity by his request, for instance, that she telephone him for the next appointment, her own self confidence might not have been as thoroughly supported as it was.

Another problem raised by Dr. Gitelson's paper which is of pedagogic importance, and which cannot be discussed at this time, is the academic distinctions allied with the terms "psychoneurosis" and "psychosis." Perhaps more time is lost in discussions among psychiatrists and more opportunity for invidious comments about each other is afforded by this confused theoretic problem than almost any other. If some frank exchange of experiences, such as the one presented by Dr. Gitelson, uncomplicated by the need to gratify so-called narcissistic goals of the discussants, were possible, it might be admitted that the chief difference between those persons who are designated as psychoneurotic and those who are called psychotic is a quantitative rather than a basically qualitative one. The functional reserve of the ego, which may vary not only from time to time but from one person to another according to his integration, would then be more generally established as the goal and the basis of prognosis.

WALTER H. BAER, M.D., *President*

Regular Meeting, April 2, 1942

Folie à Deux: Report of a Case. DR. HARRY E. AUGUST, Detroit.

In the greater part of the older literature, folie à deux represents an illness in which an originally psychotic person imposes his illness on others, usually of the same family, who are predisposed to such imposition by reason of a common defective heredity. Since 1920 a more dynamic conception has developed, namely, that the second person identifies himself with the originally sick one and expresses this

identification by taking over the psychosis of the first patient. The nature and purpose of such an identification vary according to the problems which are being solved by the use of this mechanism.

In the case presented, identification between mother and daughter had the purpose of holding in abeyance and protecting against hostile attitudes which really dominated the ambivalent relation between them. This made it possible for them to live together in apparent harmony while each was conducting her own affair in secret. When, after ten years of such an arrangement, the daughter fell in love with another man, the balance which had been maintained previously was upset, and the daughter fell into a depression, during which the mother staunchly supported her.

Immediately after the daughter's recovery, in fact, on the day of the daughter's return home, an acute agitated depression developed in the mother, in which she expressed both extremely hostile attitudes toward the daughter and a great deal of self accusation. The mother felt that she must die because of her sins, and she did die after about three months of illness. After this the daughter had a second psychosis, but one entirely different from the depression. In the second illness she made a very sharp, severe regression, with soiling, babbling, need to be fed, etc. She insisted that I was God and she was the Christ child. Her recovery constituted a rebirth, in which she was purified from her former sins and hostile attitudes. Since then she has made an excellent adjustment in her marriage and in her work.

DISCUSSION

Dr. Francis Gerty, Chicago: This is a stimulating paper for two reasons: First, Dr. August has not contented himself with a descriptive treatment of mental disturbances which appear concurrently in two or more members of a group who are interdependently related to one another by feeling, and usually by blood and common experience, but has sought rather to explain how such disturbances come about. Second, in attempting to explain what happens, he has brought out the fact, which many must have observed, that the frequency with which the same sort of mechanism is to be found in several persons in a group is much greater than that of the striking double and triple displays which these mechanisms may simultaneously release in two or three persons of the group. To express it differently, an underlying unifying stratum may be found, even though an upheaval has not caused outcropping.

It is to be regretted that Dr. August was unable to gather all the factual material he needed to sustain by a nicely constructed chain of evidence his thesis of identification, involving complementary alliance, conscience projection, revenge, guilt and expiation. In multiple cases the difficulty of doing this is extreme, especially if one patient makes a practical sort of recovery through shock treatment without revealing even facts which seemed to lie close to the surface and the other patient dies before recovery from the psychosis. Nevertheless, the hypothesis is reasonably well sustained.

In everyday life identification is common enough. Hero worship, with emulation and pleasure in sacrifice for the hero, is in a wider sphere balanced by hostility, as often submerged as expressed. The same sort of thing might logically be expected in the individual. Love and hate are more easily exchangeable than indifference is for either. In the frankly psychotic person the aberrant expressions are still more striking because they are less guarded. In cases of folie à deux it has always seemed to me that there is something of protective alliance against an unfriendly world, but with a good deal of internal conflict among the allies.

I am pleased that the matter of the neuroses has been brought up in this connection. Taking as the standard Dr. August's view of the coexistence of the mechanism rather than simultaneous display, the psychoneuroses offer the best examples of multiple mental disturbances in a group. Here commonly there are alternating displays, and I have seen husband and wife, mother and daughter,

steal the scene from one another. Sometimes a therapeutic effect of a sort is obtained when one person's illness makes it necessary for another to get better. I have recently undertaken the management of the case of a young married woman who for a year has been unable to go out on the street alone, who feels safest if her mother or her husband accompanies her, who went into a veritable panic and called in a strange woman from the street when she discovered that her mother, who lives in the next apartment, had gone out. Some suggestive points in her history are these: She is an only child. Her mother has been sick with some unusual sort of heart disease, which has existed since shortly after the birth of the daughter. The attacks lasted a few days or weeks and rallied the husband and daughter to the bedside every so often. She had one the night the daughter married, so that the daughter could not go on her honeymoon. The daughter's husband, according to the daughter (who is the patient), is unduly attached to his own family. About a year after marriage he became afraid of being alone on the street. She accompanied him as often as possible. After many months of tension and struggle he fought his illness out and became better, just as she began to have almost exactly the same sort of symptoms, but in much worse form. Now the mother (though she still regards herself as sick) has had no heart attacks for over a year, lives in the same building with the daughter and goes every place with her in the daytime, while the husband relieves in this duty at night.

Dr. Jules Masserman, Chicago: It may be useful to formulate interpersonal relationships, including the concept of identification as used by Dr. August, on fundamental psychobiologic grounds. One person influences another not by some sort of remote, quasispiritual control, but by representing a meaningful complex of fantasies and satisfactions in the other's solipsistic universe. Thus, the baby at first "loves" the mother not as a "person" but primarily because it needs her milk and care; conversely, the mother cherishes or hates the baby, depending on what it represents in her conscious and unconscious mentation. Later, the growing child still does not directly "identify" with his parents, but may, in fantasy, orally incorporate them and behave like them in an attempt to master his own toys or playmates. In this sense identification represents a changed reaction to the meanings with which a person invests his individual universe, and, more generally, "interpersonal relationships" acquire fundamental biologic and field motivational definition.

Dr. Norman A. Levy, Chicago: Dr. August is to be commended for giving a dynamic formulation of folie à deux. To describe one's patients does not clarify the situation much. Dr. August has attempted—admittedly partly as speculation—to arrive at a really dynamic understanding of what has been happening to such patients with this disturbance. It helps one to understand in similar cases that such people are reacting to each other emotionally. I was happy to see him stress the factor of identification. I have now under my care a woman in whom one can see folie a deux *in statu nascendi.* Her sister had a paranoid psychosis and was in the Elgin State Hospital. She viciously attacks my patient, who is and has been from early girlhood masochistic and overconscientious, with an extremely severe conscience, and has always taken the burdens of the family on her shoulders. This is fertile soil for accepting as real all her sister's unfair accusations. One can see in this woman the development of what later would be a paranoid psychosis, based on her guilt feelings and on an obviously strong identification with her sister.

Dr. L. J. Meduna, Chicago: In spite of the fine analysis of the 2 cases, the author did not convince me that the disorder is folie à deux. According to the accepted definition, this condition is a psychic infection of one or more members of a group or family by another member. The essential element of this phenomenon is that the disease of the first patient causes, produces or precipitates a similar or identical disease in other members of the group. This causal connection is to be considered the decisive factor. But in Dr. August's cases 2 psycho-

pathic members of the same family became ill under similar circumstances and under similar stress. It is interesting that mother and daughter had similar conflicts which produced a similar disturbance in each, but the two diseases are not interdependent; on the contrary, they developed independently of each other. So I do not think that the reported cases are instances of folie à deux.

DR. HARRY E. AUGUST, Chicago: The point Dr. Gerty made about the frequency of neurosis à deux is well taken, since often it is possible to understand certain types of neurotic symptoms only through a knowledge of the relationship of the patient to others with whom he is identified.

To answer Dr. Meduna in detail would require a repetition of much of my paper; the case Dr. Levy cited has already covered this. Dr. Meduna mentioned 3 cases in which separation of the two persons led to the relief of the illness in the one on whom it had been imposed. It is a fact that this sometimes occurs, although comparatively rarely. This, however, does not prove that the illness has been imposed. Instead, it is evidence that the identification is a comparatively loose one and that when the two persons are separated, the identification no longer holds with the same intensity.

With regard to Dr. Masserman's objection to the use of the term identification as being merely another word, identification is a definite concept. It represents a method of dealing with the relationships between people. In the case I cited it had the purpose of holding their hates in check and enabling them to live together, at first through the affairs in common and then through the psychotic reactions.

Physical Risks in Convulsive Shock Therapy. DR. VERNON L. EVANS, Aurora, Ill.

At Mercyville Sanitarium no patient has been refused convulsive shock therapy because of physical risks when it was thought that the treatment might be valuable from a psychiatric standpoint. A certain mortality was expected, just as one expects a mortality with surgical procedures. However, in many cases in which the risk was thought to be great the patients were kept on prolonged conservative treatment in the hope that shock therapy could be avoided. Several patients were treated when the risks seemed to be great. Seventeen patients were over 60 and 5 over 70 years of age. The average number of convulsions was 14.9 per patient.

The patients were treated on an ordinary bed with an ordinary mattress. No mechanical restraints and no curare or spinal anesthetics were used, but at least four attendants were required at each treatment to hold the patient and prevent abnormal movement and to check the forward lunge which causes vertebral fractures. In the case of electric shock therapy the bed was insulated and the attendants wore rubber gloves to prevent their being shocked.

Among the patients treated were 7 persons who were malnourished to the point of emaciation. Four patients were desperately ill and nearing exhaustion from excitement and increased motor activity. One woman had general osteoporosis with compression fractures of several of the vertebrae before shock therapy was started. This patient sustained an impacted fracture of the surgical neck of the humerus during her third treatment. After the fracture had healed, 6 more convulsions were induced with no recurrence of this fracture, and roentgenograms of the dorsal portion of the spine taken before and after treatment showed no additional vertebral fractures. The patient recovered from involutional melancholia, which had failed to respond to one year of conservative treatment, and she has now returned to teaching school. Another patient, a woman 74 years old, had evidence of complete left bundle branch block in her electrocardiogram. After a year of conservative treatment for the depressed form of manic-depressive psychosis, she was given 20 electric shock treatments, with no complications and with recovery from her depression. Two women over 60 years of age had systolic blood pressures over 200 mm. of mercury and were given electric shock treatment

without incident. One woman aged 54 with involutional melancholia and reactive depression had myxedema. Her electrocardiogram showed inversion of the T waves in leads I and IV and flattening in leads II and III. The basal metabolic rate was —40 per cent. She was given 4 grains (0.26 Gm.) of desiccated thyroid daily, after which the T waves became upright and of fair amplitude; electric shock treatment was then administered, without incident and with improvement in her mental condition. The only other complication was another fracture of the humerus, in an emaciated woman aged 54 with a psychoneurosis of several years' standing. A man aged 59 died of pneumonia after his second treatment. It was thought that his death, the only one in the series, was not due to the treatment but had occurred during its course because of his debilitated condition. In this series of cases the effect on the mental disease did not differ materially from those reported by numerous authors. The depressed patients responded well. In a small group of schizophrenic patients there were no recoveries, but some showed definite improvement. A few patients with the manic type of manic-depressive psychosis were treated, but the results were disappointing. A few psychoneurotic patients received the therapy, with some improvement. When the treatment of the last group of patients was undertaken, it was fully expected that there would be some serious complications and untoward results, but they were surprisingly few.

DISCUSSION

DR. CHARLES READ, Elgin, Ill.: This paper on shock therapy is unique in that it deals exclusively with an elderly group of patients. The average number of convulsions reported seems rather high. From our clinical experience and certain animal experiments, my associates at Elgin and I have come to the conclusion that the safe number of induced convulsions is probably between 10 to 12 seizures, but of course this opinion has been arrived at rather recently; at one time we treated some patients with from 25 to 50 seizures. I appreciate Dr. Evans' definition of improvement. Sometimes it seems that patients should be listed only as much improved or greatly improved, for, after all, one's psychiatric insight is, by necessity, somewhat limited in attempting to differentiate recovery or complete remission and "social" recovery. Dr. Evans' results with the involutional depressions agree with ours. Of 13 patients he reported, 11 recovered or were much improved, and the same percentage seems to hold for the manic-depressive types who were in a depression. Here again our experience at Elgin agrees with Dr. Evans'. Even though his series of manic-depressive patients in the manic state is small, we agree that the manic state is less amenable to treatment but that recovery or remission does occur. I am much pleased with the statement that no patient was refused convulsive shock therapy because of physical risks when it was thought that the treatment might be beneficial. That is a courageous attitude when one is dealing with sanatorium patients, and it reflects well on the private institution that does not hesitate to take risks when it seems they should be taken. At Elgin we are much in accord with Dr. Evans with respect to the need of desperately ill patients, those who are starving themselves or are greatly excited, provided the treatment will not do greater harm than the natural progress of the psychosis. I could cite instances of this kind in our experience to illustrate this, as well as cases in which high blood pressure is concerned. I am interested in the comment on memory defects. It is stated in the literature that patients who have had convulsive shock treatment show memory defects that are permanent or semipermanent. That has not been the observation of Dr. Phyllis Wittman in a careful study of a considerable number of patients some time after treatment.

DR. VICTOR GONDA, Chicago: It seems daring to use convulsive therapy with patients who have passed the age of 50, many of them with high blood pressure and severe myocardial damage. I have known some such patients who suffered so terribly that for many years other types of treatment were tried without result.

Dr. Evans gave electric shock treatment, of course, with the consent of the patient's family. It is gratifying to hear that relatively few complications were encountered, and especially that so many patients were benefited. I can testify here that the benefit to those patients whom I had the opportunity of observing far overweighed the complications. This paper may be an important contribution in another respect also, for it may help to solve the question whether many severe manifestations thought to be caused by organic changes in the brain, and thus to be irreparable, can be removed by convulsive treatment.

The optimal number of treatments is not known. It can be stated that fewer convulsions are needed in the cases of involutional and manic-depressive psychosis than in cases of schizophrenia.

The personnel does not need to wear rubber gloves to prevent painful shocks, for, except from the face of the patient when it is wet, there is no passage of electric current to shock any one who holds the patient, even with bare hands.

DR. LLOYD H. ZIEGLER, Milwaukee: Dr. Evans is to be congratulated on his courage in treating this group of patients, for some of whom the risk seemed to be considerable. My associates and I, too, have treated many patients over 60 and a few over 70 years of age, but few have had the physical hazards of some of Dr. Evans' patients. I want to mention briefly the complications arising from shock which we encountered. In 1 patient old endocarditis flared up and has not yet subsided. The patient had had rheumatic fever in childhood. One or two patients with arthritis became much worse after the shock unless protected by curare. In 1 patient acute glaucoma developed. A gastric ulcer bled after a shock. One patient had considerable memory defect a year after electric shock therapy. A man over 70 died after an electric shock. Necropsy showed that the myocardium was badly damaged and the stomach greatly dilated. Tuberculosis of the lungs is said to be activated by shock, but we have had no experience with it. We treated a patient with a blood pressure of 220 systolic and 120 diastolic without trouble, but he did not recover. Treatment of a patient who two or three years previously had had a subarachnoid hemorrhage gave no untoward results, but he was not benefited. A man aged 68 who was known to have had an attack of coronary thrombosis several years ago responded well to the therapy. We have treated extremely emaciated patients, some of whom gained weight rapidly.

We find that 8 to 12 shocks is all that is necessary to obtain results.

DR. VERNON L. EVANS, Aurora, Ill.: The average number of convulsions which my associates and I employ has been increased by a few cases in which treatment was prolonged. In 1 patient, with old schizophrenia, we induced about 75 convulsions. The treatment was given chiefly to please her daughter, as the patient was so good when under therapy and so bad without it. Another patient, a man aged 72 who has been depressed, is receiving perennial treatment. When he came in I thought he had senile psychosis, as he seemed so confused and oblivious of his surroundings. He responded well, went home and in a few months came back again in a depressed state. We gave him electric shock; he responded again and now comes in about every two months. During one of the intervals he gave himself up at the local jail, asking that he be isolated so that he would not contaminate the other prisoners. He does not have to be tube fed now (as he did); he works in his garden and gets along with occasional bolstering from treatment. A few cases, then, have raised our average number of convulsions rather high. Like Dr. Gonda, we give fewer treatments and find them adequate in most cases.

We, of course, should like to avoid treating emaciated patients when we can, but in some cases it seems best to go ahead with the treatment, when despite tube feeding and other measures the patient does not seem to be gaining ground.

The patient with thyroid disease had myxedema, but the T waves in her electrocardiogram became upright and her metabolic rate rose to normal with the administration of thyroid.

With regard to heart disease, at present we have a patient, not included in this report, who has arteriosclerotic heart disease with auricular fibrillation, but no decompensation. She has received 3 convulsive shocks, with no visible ill effects to date.

CHICAGO NEUROLOGICAL SOCIETY

ROY R. GRINKER, M.D., *President, in the Chair*

Regular Meeting, March 19, 1942

Pseudotumor of the Brain: Report of a Case. DR. MABEL G. MASTEN, Madison, Wis.

The case of a girl aged 15 years is presented as a diagnostic problem. During March and April 1938 she had several attacks of lancinating pain over the left eye, with vomiting and drowsiness; between attacks she was well. She was admitted to the Wisconsin General Hospital on the eighth day of the last attack. She had had chronic otitis media involving the right ear since the age of 11 years, when a bilateral paracentesis was done.

Neurologic examination revealed inequality of the pupils, the left being larger than the right, marked choking of the disks, tenderness over the exits of the cranial nerves, suppression of tendon reflexes and a right upper quadrant defect in the visual fields. Roentgenograms showed extensive sclerosis of the right mastoid and good aeration of the cells of the left mastoid, but with thickening suggestive of early chronic infection. No abscess could be detected in the left petrous pyramid. The spinal fluid pressure was elevated. The fluid contained no cells; the protein was increased, and the colloidal gold curve was 3343210000. The blood count showed 17,700 leukocytes, 80 per cent of which were polymorphonuclear cells. Purulent exudate was noted in the right external auditory canal, but the left canal was dry. Both drums were perforated. A ventriculogram showed pronounced displacement of the ventricles to the right, with deformity of the body and temporal limb of the left ventricle, suggesting a space-filling lesion of the left temporoparietal region.

An exploratory craniotomy was done, but the dura was so tense that it was not opened. Aspiration with a needle failed to yield pus. Choking of the disks increased. A tube was placed in the right lateral ventricle, and after further dehydration reexploration was carried out. The dura was still too tense to permit its being opened, and the bone flap was replaced. Subsequently, the patient received high voltage roentgen therapy and made a good recovery. On reexamination six months later she stated that she had been well; the disks were no longer choked, but the defect in the visual fields persisted.

She was admitted to the hospital two years later, after having had three isolated convulsions. There were no clinical symptoms. An encephalogram revealed some enlargement but no displacement of the ventricles. The cortex was well outlined on the right, but poorly delineated on the side of operation. The left ventricle, especially the temporal limb, was slightly larger than the right. There has been no recurrence of convulsions, and the patient has remained well to date.

This case is reported because it presents all the clinical features of a space-filling lesion of the left temporal lobe. Tumor could be dismissed from consideration. On the basis of the encephalographic signs, it is suggested that a localized infectious process, possibly the result of an undisclosed petrous abscess, had been recurring without reaching the stage of necrosis and walling off, remissions being aided perhaps by roentgen therapy. Reactive edema of the hemisphere may have been responsible for the pronounced shift of the ventricles. The convulsions were

assumed to be a postoperative complication. (Lantern slides of encephalograms and ventriculograms were shown.)

DISCUSSION

DR. NORMAN A. LEVY: I wonder whether this case may not have been one of nonsuppurative encephalitis. There arises the question of the occurrence of cerebral edema, or so-called hydrocephalus, during the course of otitic infection. In cases of cerebral edema the ventricular system is small and is not distorted, as the edema is apparently diffuse and symmetrically distributed. In the present case the pathologic alterations were predominantly unilateral and may have been due to diffuse nonsuppurative encephalitis with concomitant edema involving chiefly one hemisphere.

DR. MABEL MASTEN, Madison, Wis.: I do not think there would be a unilateral process with such extreme choking of the disks in encephalitis. I assume that the edema compressed the cavernous sinus. The lesion could not have been a walled-off abscess. Might it have been, however, a suppurative process in which encapsulation had not developed but in which resolution occurred, with residual scar tissue in the hemisphere? The dilatation of the body and temporal limb of the left ventricle suggests atrophy secondary to such a healing process.

Relation of Cerebral Cortex to Basal Ganglia. DR. WARREN S. MCCULLOCH.

Many years ago Dusser de Barenne mapped the sensory cortex by local application of strychnine and observations on clinical behavior indicating disturbances of sensibility. Since strychninization of 1 sq. mm. of any part of any somatotopic subdivision was sufficient to induce hyperesthesia or paresthesia and paralgesia of the entire corresponding portion of the body, he formulated two hypotheses: (1) Such strychninization "fired" all parts of that subdivision of the cortex, and (2) the strychninization "fired" the corresponding thalamic nucleus. Both hypotheses were amply confirmed years later by local application of strychnine supplemented by recording of the electrical activity of the part in question.

The combined technics showed that strychnine acts only where synapses are present on cell bodies and that it causes these cells to "fire" synchronously, with the production of sudden spikelike discharges, which can be recorded from any structure to which the strychninized cells send axons or collaterals. By these technics the functional organization of the sensory cortex was mapped. In so doing, a new phenomenon was encountered. With the animal under dial narcosis the cortex remains spontaneously active even after decapitation or decerebration, but its so-called spontaneous activity is immediately stopped if the cortex is severed from the thalamus. Focal lesions of the sensory nuclei of the thalamus have a similar effect, but one which is localized to the corresponding part of the cortex. Local strychninization of any one of four narrow strips of cortex was found to produce transient diminution or loss of this so-called spontaneous activity. From before backward, they are Brodmann's areas 8, 4-s, 2 and 19.

The suppression of electrical activity which these areas yield does not depend on corticocortical connections, as can be shown by antecedent severance of such pathways. It does depend on corticostriatal projections, for destruction of the nucleus caudatus prevents it and actually permits increased amplitude of cortical activity. Moreover, strychninization of areas 8, 4-s and 2 causes "strychnine spikes" to appear in the nucleus caudatus.

These observations led to a study of the corticostriatal connections, with strychninization of all parts of the cortex and placing of pick-up electrodes in all parts of the corpus striatum. The results were without significance except for the following observations: Area 8 (suppressor) projects to the caput and the anterior part of the cauda of the caudate nucleus; area 6 projects to the putamen and to the external segment of the globus pallidus; area 4-s (suppressor) projects in part to the caput, but chiefly to the horizontal portion of the cauda; area 4

projects to the putamen alone, and, finally, as shown in one unexpectedly successful experiment, area 2 (suppressor) projects to the thin posterior portion of the cauda of the nucleus caudatus, just as it starts to descend. So far I have not been fortunate enough to place an electrode in the descending portion to which one would expect area 19 (suppressor) to project.

All the foregoing observations were made on monkeys. More recently they (except those with respect to area 2) have been confirmed on chimpanzees.

Examination of all the available data on the corticostriatal projections shows no evidence of somatotopic localization, for face, arm and leg subdivisions are represented in each structure in profusion and without apparent arrangement. What examination does show is a corticotopic localization, with the suppressor areas projected on the nucleus caudatus, the motor area, 4, on the putamen, and the premotor area, 6, on the putamen and the external segment of the globus pallidus.

DISCUSSION

DR. A. EARL WALKER: The conceptions of the function of the basal ganglia which Dr. McCulloch has so clearly presented are quite in line with those suggested by Kinnier Wilson. They represent a distinct innovation in the concept of the physiology of these structures, with a sharp turn from the former view that the basal ganglia constituted some sort of extrapyramidal motor system acting on the lower motor neuron. It was Kinnier Wilson's impression that the basal ganglia influenced the cerebral cortex in man and the higher primates. Dr. McCulloch and his associates have fully confirmed that hypothesis. The experimental studies of Kennard and Fulton in the production of choreoathetoid movements and tremor point in the same direction. Mettler's experimental demonstration that stimulation of the caudate nucleus inhibits motor phenomena elicited from the cerebral cortex is a further line of evidence. All this experimental work, which fits together so well, suggests that the mechanisms by which the basal ganglia influence the motor activity are beginning to be understood.

DR. WARREN S. MCCULLOCH: I wish I felt as sure as Dr. Walker does that this work was going to make much sense with regard to the motor phenomena. One would expect the observations to fit in with what is known of the corticostriatal system, but they do not. There are two or three slides which may help clarify my studies on this problem. They show that the suppression of motor response to cortical stimulation, although it can be produced by stimulation of area 4-s and can be prevented by undercutting of that suppressor area, remains when the nucleus caudatus is pithed, the substantia niger is pithed bilaterally or the cerebellum is ablated. Hence it is obvious that no one of these structures, singly, is necessary for suppression of motor response. This is the more surprising, as stimulation of the nucleus caudatus, for example, produces such suppression.

Sexual Precocity Associated with Hyperplastic Abnormality of the Tuber Cinereum: Report of a Case. DR. I. P. BRONSTEIN, DR. JOSEPH A. LUHAN and DR. WILLIAM B. MAVRELIS.

REPORT OF A CASE

A girl 22 months of age exhibited vaginal bleeding, enlarged breasts and vulval hair. The possibility of involvement of the hypothalamic apparatus was entertained. Intracranial symptoms were not present. In pneumoencephalographic studies, visualization of the ventricles and cisterns revealed nothing abnormal. The child died of meningitis due to Bacillus pyocyaneus.

A detailed postmortem examination was made. In the region of the tuber cinereum a globular, grayish white, glistening mass, about 4 mm. in diameter, was observed in the midline just in front of the mamillary bodies. The pineal

body appeared normal. Histologic examination of the tumor showed that it resembled in structure the tuber cinereum, and the diagnosis of a hyperplastic malformation (hamartoma in the sense of Albrecht's definition) rather than of ganglioglioma or pseudoheterotopia. The pituitary presented relative hyperplasia of the eosinophils of the pars distalis. Except for these alterations, the endocrine system was normal to macroscopic and microscopic inspection.

The relation of the mass to the sexual precocity is discussed. The various mechanisms responsible for this phenomenon are postulated.

DISCUSSION

DR. ARTHUR WEIL: Through Dr. Luhan, I had the opportunity of studying both the gross specimen and the serial sections in this case. I agree that one should not call this protrusion of brain tissue at the base of the tuber cinereum a neoplasm. It was well encapsulated by meninges and showed the same structure as the tuber cinereum, with a marginal zone of glia and a center which contained neurons, resembling those in certain other nuclei of the hypothalamus. The lesion might be called a malformation, a displacement of brain tissue or a hamartoma.

This case is an exact duplicate of the case of a boy 3 years old described by Driggs and Spatz (*Virchows Arch. f. path. Anat.* **305**:567, 1939). They, too, emphasized that the malformation was not a neoplasm. They discussed the probability that increased "neurosecretion" of the tuber cinereum might have been responsible for the sexual precocity, and they referred to Scharrer's work on the hypothetic production of hormones in ganglion cells. They cited 10 instances of pubertas praecox in which the hypothalamus alone was diseased. One of these cases (Heuyer and Lhermitte) was similar to their own and the one presented here. In 3 of the cases a large glioma invaded both the hypothalamus and the mamillary bodies or filled the third ventricle (Schmalz; Horrax and Bailey; Saar); 1 was a case of carcinoma of the third ventricle (C. Schmid), and another, a case of a mixed tumor arising from the choroid plexus. In 4 cases the condition was associated with encephalitis (3 cases of Ford and Guild and 1 of Hellner). Dott, in his Henderson lecture of 1938, described a case of this kind.

In view of this variety of pathologic processes, it is hard to believe in an excessive physiologic neurosecretion as the etiologic factor responsible for the sexual precocity. The disturbances of development or the destruction of the region of the tuber cinereum by tumor or encephalitis suggests rather the elimination of a nerve center which is essential to the proper balance of sexual development. That such centers really exist in the hypothalamus has recently been demonstrated experimentally by Dey and Ranson and their associates. These investigators observed that in the hypothalamus of the guinea pig two areas exist, destruction of one of which leads to constant estrus and destruction of the other to atrophy of ovaries and uterus and to disturbance of the estrous cycle. I am sure that Dr. Dey will describe these experiments in detail.

DR. FREDERICK L. DEY: My associates and I (Dey, F. L.: Changes in Ovaries and Uteri in Guinea Pigs with Hypothalamic Lesions, *Am. J. Anat.* **69**:61, 1941. Dey, F. L.; Leininger, C. R., and Ranson, S. W.: The Effect of Hypophysial Lesions on Mating Behavior in Female Guinea Pigs, *Endocrinology* **30**:323, 1942) have found that lesions placed in the anterior portion of the hypothalamus of female guinea pigs may prevent the secretion of luteinizing hormone. As a result the ovaries become follicular but are lacking in corpora lutea. The uterus increases greatly in size. Lesions that destroy the median eminence, on the other hand, abolish ovarian cycles, and the ovaries and uterus atrophy. In these animals it appears that the follicle-stimulating hormone is deficient. These results cannot be attributed to direct hypophysial damage, since lesions that are placed directly in the hypophysis and which destroy as much as two thirds of the parenchyma of the anterior lobe of the pituitary do not alter the sexual cycle. Moreover,

interruption of the hypophysial stalk soon after it leaves the hypothalamus also fails to alter the sexual cycle.

It appears, then, that the hypothalamus may play an important role in regulating gonadotropic functions of the pituitary. Our results indicate that the anterior portion of the hypothalamus is concerned with the elaboration of luteinizing hormone, while the more caudal portion of the hypothalamus is concerned with the elaboration of follicle-stimulating hormone. The manner in which these hypothalamic areas affect function of the pituitary is vague at present; however, it is probable that the median eminence plays an important role in the mediation of this control.

It may be significant that in the case of pubertas praecox just presented the median eminence was described as being "hyperplastic and highly vascular."

Dr. L. M. Weinberger: The authors are to be congratulated on their thorough study of this case. As a matter of fact, few studies have equaled it, and certainly none have exceeded it, in detail. Such rare cases have both a positive and a negative value—positive in that they point to the hypothalamus as the critical structure concerned in the causation of precocious puberty, and negative in that they serve to dispel the myth that the pineal body has anything to do with this phenomenon. Tumors of the pineal body compress or destroy the hypothalamus, but only in this way are they causal.

That disease of the hypothalamus is the cause of precocious puberty is not a new idea; almost twenty years ago Buescher suggested that the mamillary bodies were concerned with sexual innervation. I think it is now adequately proved that lesions of the anterior part of the hypothalamus result in hyposexuality and gonadal atrophy, possibly because they interfere with a mechanism which normally serves to excite the pars distalis of the pituitary gland. On the other hand, lesions of the posterior portion of the hypothalamus appear to cause hypersexuality and gonadal hypertrophy because they destroy a mechanism which ordinarily serves to inhibit the activity of the pars distalis. Endocrinologists agree, I believe, that the output of gonadotropins from the pituitary gland are the sole activators of the gonads. This being true, it appears that however the hypothalamic lesions exert their effects, they must act on the pituitary gland first. The pituitary gland must be thought of as the effector organ of the hypothalamic mechanisms so far as sexual development is concerned.

Many questions concerning the neuroendocrine basis of precocious puberty are still unsolved, but studies such as this indicate that a neural mechanism or mechanisms are located in the floor of the third ventricle which control the rate and amount of discharge of the gonadotropic principles from the pituitary gland.

Dr. Percival Bailey: It is not logically necessary to assume that two mechanisms are operative in producing genital hypoplasia and genital hyperplasia with lesions of the hypothalamus. Only one mechanism may be overactive or underactive, as the case may be. However that may be, sufficient cases are now on record to prove that a tumor of the hypothalamus may produce precocious puberty in the presence of an apparently normal pineal body.

I doubt whether there was eosinophilic hypertrophy of the hypophysis in this case. Such an assertion is difficult to prove. The literature is full of unwarranted assertions concerning the proportion of chromophil cells in the anterior lobe of the hypothysis.

Dr. I. P. Bronstein: I avoid the term precocious puberty because to me it has the connotation of rhythmicity. Albright of Boston, in a personal communication, stated that disturbances of the hypothalamus are the only cause of true precocity in females.

I was much interested, in going over the literature on the hypothalamus, to note Uotila's comments on the existence of corticohypothalamic and hypothalamicohypophysial fiber tracts and the possibility of their eventually explaining how mental disturbances can affect the functions of the anterior lobe of the pituitary.

I make the point that lesions other than actual tumors and abnormal growths, e. g., germ plasm defects, may produce such aberrations. I started to study a boy five or six years ago. He is mentally deficient, and, just as he has mental retardation, he may have a defect of the germ plasm which causes the sexual precocity. The state of the pituitary body in hypergonadal conditions is not certain.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

H. Houston Merritt, M.D., *Presiding*

Regular Meeting, April 16, 1942

Myoclonus Epilepsy: Report of a Case, with Presentation of a Moving Picture and Anatomic Slides. Dr. Paul I. Yakovlev, Waltham, Mass.

I wish to show moving pictures of a patient with progressive myoclonus epilepsy, whose history I shall relate later. A young woman, bedridden by weakness, contractures and gross incoordination, displayed spontaneous, nonrhythmic jerks and starts, occurring now and then, here and there, in her arms, shoulders, head and legs. At certain times these jerks grew in intensity and frequency until they became violent, rhythmic and symmetric and eventually culminated in an epileptic fit. All voluntary movements, such as those displayed in a finger to nose test, were slow in starting and, once initiated, were distorted by asynergic myoclonic contractions. Ocular and facial movements were affected by similar incoordination.

The cinematograph was taken shortly after the patient came under my observation, at the age of 27, about three years before her death. A maternal aunt suffered from epilepsy. The patient had had bilateral pes cavus since infancy. At the age of 12 her gait became slightly incoordinate. At the age of 17 she had her first epileptic fit. Her movements were increasingly impaired by sudden myoclonic contractions in the arms, shoulders and legs, and she became unable to feed herself. At the age of 26 she fell and dislocated her left knee and since then had been bedridden.

Neurologic examination on admission revealed severe muscular rigidity of proximal distribution, masklike facies, contracture in flexion of the lower extremities and a bilateral Babinski sign. As the disease progressed, rigidity and flexion contractures increased, with involvement of the upper extremities as well. She became demented and died of bronchopneumonia at the age of 30, after an illness of at least eighteen years.

Pathologic Observations.—Pronounced atrophy of the brain stem and cerebellum was evident grossly. The fourth ventricle was enormously dilated as a result of atrophy of the tegmentum, the roof nuclei, the superior cerebellar peduncles and, especially, the dentate nuclei. The dentate nuclei showed aplasia and sclerosis. The inferior olives had undergone a moderate degree of pseudohypertrophic atrophy. Capsule fibers of the olives and the central tegmental tract were pale. On the contrary, olivodentate fibers were well stained and could readily be traced through the restiform body into the capsule of the dentate nucleus. The medial lemniscus and the medial longitudinal bundle were pale and atrophic. The spinocerebellar fibers and the nuclei and tracts of Goll were selectively bleached. The same was true of these tracts in the spinal cord. In addition, there was some pallor in the ventromedial funiculi, where the vestibulospinal and the tectospinal fibers ran.

The cerebellar cortex showed widespread atrophy of a remarkably spotty distribution. The neocerebellar parts were most affected, especially their ventro-

medial portions. The vermian lamellas were relatively spared. However, even in the hemispheres some lamellas were spared, while others nearby were atrophic. The atrophy was histologically selective. It was a characteristic centrifugal degenerative type of cortical atrophy, for it affected the Purkinje cells and spared their baskets. The dentate nucleus showed gliosis and characteristically spotty loss of cells. Some coils had lost almost all their cells, while others nearby were relatively spared.

The cerebral cortex showed no cytologic changes. Huge amounts of amyloid material were heaped in the subcortical white matter of the centroparietal region of the hemispheres, forming there a distinct purplish line, visible in Nissl preparations with the naked eye. In the thoracic portion of the cord the amyloid bodies were deposited selectively in Clarke's nucleus. The Turnbull stain for iron, carried out on serial sections, revealed that the pallidum, the substantia nigra reticulata and the dentate nucleus were selectively loaded with huge amounts of iron pigment and melanin. Blue granules of iron pigment were scattered free in the tissue of these structures, heaped about broken-down nerve cells and deposited in perivascular and subarachnoid spaces.

Comment.—The pathologic changes in progressive myoclonus epilepsy are diverse. The localization of symptomatic components of the disease is, on the contrary, remarkably consistent. In the case reported two symptomatic components must be distinguished—the myoclonus and the syndrome of neurosomatic deterioration, viz., rigidity, flexion contractures and dementia.

The rhythmic, branchial myoclonus and the nonrhythmic, skeletal myoclonus have a common localization in the myoclonic triangle of the hindbrain, formed by the central tegmental tract as its base, the inferior cerebellar peduncle as its caudal side and the superior cerebellar peduncle as its rostral side and the dentate nucleus as its apex. The lesions associated with rhythmic, branchial myoclonus emphasize the inferior olive, the base and the caudal, or cerebellopetal, side of the triangle. The lesions associated with nonrhythmic, skeletal myoclonus emphasize the rostral, or cerebellofugal, side of the triangle. The nonrhythmic myoclonic contractions of skeletal musculature, scattered in time and space, affecting a muscle or a portion of a muscle, may be looked on as a special form of cerebellar asynergia. The clinical features of the myoclonus appear to stand in relation to the characteristically spotty, disseminated degeneration of the cerebellofugal system, involving selectively the layer of Purkinje cells, the dentate nucleus and the superior cerebellar peduncle. The skeletal myoclonus may be considered, therefore, as asynergia of the motor units, rather than of the large groups of muscles, as is observed with massive, nonselective, wholesale atrophy and lesions of the cerebellum.

In rare cases of skeletal myoclonus not complicated by epilepsy, rigidity and contractures, the lesions as a rule are confined to the hindbrain. Such are the classic cases of Hanel and Bielschowsky, of Pilotti and of Prechechtel. On the contrary, in cases of myoclonus associated with epilepsy, rigidity and flexion contractures, the pathologic process shows a rostral extension into the diencephalon, the pallidonigral system being particularly involved. From the standpoint of the evolution of symptoms and localization of lesions, the case reported appears to conform to the argument just presented.

DISCUSSION

DR. WILLIAM G. LENNOX: I wish there were more careful case studies of this sort. I was a bit surprised to hear Dr. Yakovlev say that myoclonus bears little relation to epilepsy. A large portion of Dr. Muskens' volume on epilepsy (Berlin, Julius Springer, 1926) is devoted to proving that myoclonus is the essential constituent of epilepsy, about 70 per cent of his patients having had myoclonic jerks before epilepsy developed. I have seen only a few patients who had myoclonic jerks without epilepsy; myoclonus is certainly a frequent accompaniment of epilepsy. In patients with myoclonic epilepsy, the muscle shocks

are coincident with a wave and spike petit mal formation in the electroencephalogram. One of our cases resembles Yakovlev's case a good deal, but the man is a member of a university faculty. This patient presented no cortical electroencephalographic changes coincident with the muscle shocks. Possibly this is evidence of involvement of the brain stem rather than of damage to the cortex.

DR. WILLIAM L. HOLT, Westboro, Mass.: Is there any pathologic relation between this myoclonia and electric chorea? In 1937, at the Massachusetts General Hospital, I saw an Italian woman of about the age of this patient. She had what resembled electric chorea. At the time I was puzzled as to whether there was some pathologic relationship between electric chorea and this form of myoclonia.

DR. H. HOUSTON MERRITT: Dr. Yakovlev showed the distribution of iron pigment, which was similar to that in Hallervorden-Spatz disease. Is there not a difference?

DR. PAUL I. YAKOVLEV, Waltham, Mass.: In reply to Dr. Lennox's question: I feel that from the point of view of localization the myoclonic contraction as a symptom of a lesion of the nervous system is distinct from the muscular contraction of an epileptic fit. Hodskins and I (*Am. J. Psychiat.* **9**:822 [March] 1930), in a survey of the literature, reviewed cases of myoclonus with and without epilepsy and with adequate postmortem study of the nervous system. In 3 cases the myoclonus was not associated with epilepsy. In 18 cases, that is, in about 85 per cent, myoclonus was associated with epilepsy and the usual clinical manifestations of what is called neurosomatic deterioration, viz., rigidity, contractures and various degrees of dementia. In all the cases reported pathologic changes were present in the hindbrain, the dentate nucleus in particular. However, in cases of myoclonus without epilepsy the pathologic changes were relatively confined to the hindbrain and showed no rostral extension into the diencephalon and hemispheres, whereas in cases associated with epilepsy, and that implies rigidity, contractures and dementia, such a rostral extension, with involvement of the cerebral cortex, thalamus, pallidum and substantia nigra, was a prominent feature. These observations, taken at their face value, permit one to assume that the myoclonus is related to pathologic processes in the hindbrain, whereas the epileptic fits, rigidity, contracture and dementia are symptoms related to a more general cerebral disease involving the hemispheres as well, and the diencephalon most of all. The case reported tonight appears to conform to the foregoing generalization.

In reply to Dr. Holt's question: It is remarkable how confusing is the terminology in use in this field of clinical neurology. For example, one often speaks of the paramyoclonus multiplex of Friedreich. If one will read the original description of Friedreich, who coined the term, one will readily see that the case he described could not be classed with any of the cases subsequently described under the name of paramyoclonus multiplex. The term, however, remained ingrained in medical literature. The same is true in regard to various so-called electric choreas such as those of Dubini, Henoch and Bergeron. Terms of this kind are purely descriptive and emphasize one or another prominent feature of abnormal muscular contraction, such as its quickness and its similarity to the contraction caused by a discharge from an induction coil or its occurrence in symmetric muscles of the extremities ("paramyoclonus"). However, an immense variety of entirely different conditions underlie this motor symptom. Perhaps the electric chorea of Dubini deserves better to be preserved as a nosographic term than the other, unrelated conditions known under the same name. It should be preserved on historical grounds, for it was probably the first description of what is now known as the myoclonic form of epidemic encephalitis, which occurred in 1846 in northern Italy and was described by Dubini. A severe febrile disease associated with somnolence preceded the condition, and in most instances the disease was fatal.

Dr. Merritt's question brings up an interesting point for discussion. There are about two score cases described in literature under the name Hallervorden-

Spatz disease. It is noteworthy that in this disease, of which the case reported is from the histopathologic viewpoint a typical example, there are, in addition to the selective depositions of iron in the pallidum and the substantia nigra, widespread degenerative lesions elsewhere in the nervous system—the cerebellum and brain stem particularly. Most authors emphasize the syndrome of neurosomatic deterioration, viz., rigidity, contractures and dementia. However, the involuntary movements are often present, at least in the earlier stages of the disease. These movements are usually described as tremor, choreoathetosis or simply *stossende Bewegungen*. It is pertinent, also, to point out that Wilson's hepatolenticular degeneration was described earlier by Ormerod under the significant term "tetanoid" chorea. Indeed, the myoclonic character of involuntary movements in Wilson's hepatolenticular degeneration is generally known. Here, again, the widespread degenerative changes in parts of the nervous system other than the lenticular nuclei —the cerebellar cortex and the dentate nuclei in particular—are often present. The myoclonus is a symptom common to many degenerative diseases of the nervous system with involvement of the brain stem.

Sympathetic Innervation of the Skin: Experimental and Clinical Studies.

Dr. Curt P. Richter, Baltimore.

In a previous paper (Richter, C. P., and Woodruff, B. G.: Facial Patterns of Electrical Skin Resistance, *Bull. Johns Hopkins Hosp.* **70**:442 [May] 1942) it was reported that by means of the electrical skin resistance method areas affected by sympathectomy could be accurately and quickly mapped on any part of the body. Sympathectomized areas had a high electrical skin resistance. In the lumbar region these patterns of high resistance corresponded closely with the patterns of the sensory dermatomes. We are thus able to determine almost at once the success of the operation; we can also detect the presence of regeneration.

With this method it was found that normal persons have several areas of low electrical skin resistance; an oval area on the face, including the eyes, nose and mouth; an area on the hand, including the palmar surface and part of the dorsal surface of the ends of the fingers; an area on the foot, including the plantar surface and part of the dorsal surface of the foot, almost up to the ankle, and areas in the axillas and the antecubital fossae.

The facial area constricts with cold and sleep until it includes only the mouth, and expands with warmth to include all of the face and head. These patterns seemed to correspond with the areas of remaining sensitivity to pain and heat found in cases of syringobulbia. The resistance inside the area is usually about one-fifth as high as that of the surrounding part of the skin. The sensitivity to electric shock and to pain is increased inside the area. Section of the trigemmal nerve alters the facial pattern.

The patterns on the hands and feet also constrict with cold and sleep, the tips of the fingers and toes being the last to show the low resistance.

With this method my associates and I have followed regeneration of nerves after peripheral injury. We have also mapped areas of referred pain; these areas show low resistance. In several hysterical patients we found glove and sock patterns on the hands and feet.

The method has the great advantage that it does not depend on the cooperation of the patient; further, the apparatus, because of its compactness and simplicity, can be used at the bedside.

DISCUSSION

Dr. James C. White: This is an interesting subject to me. Dr. Finesinger, Dr. Smithwick and I have been studying changes in electrical skin resistance in sympathectomized patients at the Massachusetts General Hospital. We have not had such a simple, effective apparatus, but we have found the method most practical. We have also employed a slight modification of the finger plethysmograph, originally described by Carmichael in England, and have found it most

satisfactory for the study of fine vasomotor reflexes. A deep breath, a sudden noise or touching the body with a pin or with cold water will produce striking vasoconstriction in a normal extremity. Distribution of sweating is another accurate method of testing the presence of the sympathetic fibers. With determinations of skin resistance, as described by Dr. Richter, we have made several observations of interest. One is that if a preganglionic sympathectomy is done and daily measurements of skin resistance are made, about the second or third day the resistance drops from several million to perhaps 30,000 ohms. This lasts only about thirty-six hours, and the resistance then increases and stays high. This does not occur after postganglionic sympathectomy. I wish I could have had this apparatus in Halifax three weeks ago, when I was studying a group of men who had been torpedoed and exposed to cold air and sea water in lifeboats. They came into the hospital with intense hyperemia and injury to peripheral nerves, with loss of sensation from the ankles down. Observations on skin resistance and its fall with neural recovery would have been a practical objective method for studying recovery of nerves injured by cold.

DR. JACOB FINESINGER: Dr. Richter's work represents an important contribution to the field of skin resistance. It seems to me that getting rid of the electrode paste in the technic of measurement has simplified considerably the problem of measurement of skin resistance. I wonder what would be the values for skin resistance in various areas with this method and with the usual technic. We have noted in our own work that certain regions of the skin, for example, the volar, or forearm, area, usually have high resistance. I wonder whether Dr. Richter could tell what happens in such areas after sympathectomy. We also have the impression that the high values for skin resistance observed after sympathectomy are not always found to persist when the area of skin is measured month after month. We should like to know whether, in Dr. Richter's opinion, this decrease in skin resistance is due to regeneration phenomena or to some other process.

DR. JAMES C. WHITE: I should like to ask Dr. Richter a question in another connection. Dr. Smithwick and I have been having an argument with Dr. Kuntz and Dr. Heinbecker, in St. Louis, about the distribution of the sympathetic fibers to the upper extremity.

We have found that after the preganglionic type of sympathectomy there is no detectable sweating over the arm, although the first thoracic and the inferior cervical ganglia are left intact. After this operation we have tested numerous patients for sweating and for electrical skin resistance, and they all have shown that the hand is completely denervated. The men in St. Louis made their studies on animals and concluded that important sympathetic fibers come out over the first white ramus communicans to reach the arm. Has Dr. Richter any evidence that in man important sympathetic pathways run to the arm from the spinal cord above the second thoracic segment?

DR. H. HOUSTON MERRITT: I should like to ask Dr. Richter whether he has ever used this method in localizing lesions of the spinal cord that do not give obvious sensory loss.

DR. AUGUSTUS ROSE: In cases of referred pain does the area of low resistance correspond to the area of hyperesthesia?

DR. WALTER WEGNER: I understood Dr. Richter to say that in hysterical patients, with an increase in skin resistance, there was also paralysis of fibers. Is not that contrary to the usual observation that such persons show increased sweating of the extremities?

DR. CURT RICHTER, Baltimore: In reply to Dr. Finesinger's question: Resistance is much higher with a plain zinc electrode. It ordinarily is about 2,000,000 or 3,000,000 ohms, and sometimes it is so high that we cannot even measure it on our machine. We have a new machine now which is more sensitive. We have found that after sympathectomy the resistance of some patients will

fall, but never near the range of normal. I do not know what the drop means. Perhaps it depends on the activity of local sweat glands or on autonomic action.

In reply to Dr. White's question: I cannot say anything now regarding the pathway from the first thoracic nerve. Before long I think we shall be able to give a definite answer, at least in monkeys, by the study of the effects produced by removal of a single ganglion or by section of individual rami.

In reply to Dr. Rose's question: We did not make any tests for sensitivity on patients with referred pain.

In reply to Dr. Wegner's question: The sock and glove patterns on the feet and hands have a low skin resistance, which is associated with increased rather than with decreased activity of the sweat glands.

Book Reviews

The Diseases of the Basal Ganglia. Research Publications, Association for Research in Nervous and Mental Disease. Vol. XXI. Pp. 719, with 268 illustrations. Baltimore: Williams & Wilkins Company, 1942.

After an historical introduction to the basal ganglia and their diseases by F. H. Lewy, a considerate, concise description of the nuclei and pathways of the basal ganglia and their connections is given by J. W. Papez. Comprehension of the complex anatomy is facilitated by carefully chosen illustrations and diagrams. The author does not attempt to cover the gaps of knowledge or to deduct functions from anatomic facts. S. W. Ranson Sr. and Jr. produced experimental lesions in the striatum and pallidum and followed the secondary degeneration of neurons with the help of the Marchi method. They show clearly the presence of a nigropallidal tract. They further note that the well known pallidosubthalamic bundle springs from the outer third of the globus pallidus and the fasciculus and ansa lenticularis from the inner third. A large number of fibers reach the thalamus over the bundles H, H_1 and H_2.

L. Alexander confirms by means of injection preparations the statement that in most persons the striatum receives its blood supply from direct branches of the anterior and middle cerebral arteries, whereas the globus pallidus, the retrolenticular substance and the cornu ammonis are usually supplied by the anterior choroid artery. It is pointed out that the artery last mentioned is one of the longest of the brain and that this may be the reason both the globus pallidus and the cornu ammonis show a specific tendency to be affected whenever the blood pressure or the oxygen supply is lowered.

D. McKenzie Rioch reports that in cats deprived of the neocortex no specific function of the striatum or the globus pallidus could be determined. He objects to such terms as sham rage, sham fear or sham pleasure. The wider variety of the behavior patterns now discovered requires a less presumptive nomenclature, in terms of the characteristic features of the individual pattern.

F. A. Mettler, from a thorough study of the literature and from his own interesting experiments concludes that the striatum occupies the position of an inhibitory mechanism on the pyramidal-extrapyramidal system whereas the pallidum represents a positive motor mechanism through which associated movement patterns are involved in tonic discharges. Mettler, in the beginning of his article regrets, correctly, that so little of the extensive European literature on extrapyramidal function has received notice in the English literature. This omission has, unfortunately, not been remedied in his article.

The article of Kennard and Fulton and the following one of Dusser de Barenne, Garol and McCulloch, dealing with the corticostriatal connections, are probably the most interesting papers of this volume. The former authors present data accumulated from observations on isolated and combined lesions in monkeys and apes; the latter utilized the strychnine-spike method in investigating the corticostriatal relationship. The first article stresses the interdependence of the cortex and the basal ganglia for coordinated complex motor actions and for the appearance of various involuntary movements resembling tremulous, choreiform or athetoid movements. These authors saw, in contrast to the observations of Ranson, marked slowing of active movements and increased resistance to passive movements after sufficiently large lesions in the globus pallidus had been produced. In the discussion of this paper it was suggested that the application of clinical terms to phenomena observed in experimental monkeys easily gives rise to confusion.

The paper of the late Dusser de Barenne and his co-workers proves again the superiority of the modern functional methods over static anatomic procedures.

The authors demonstrate unequivocally that the strip areas in front of areas 4 and 6 and in the postcentral area, stimulation of which suppresses motor action from stimulation of area 4, send their neurons directly to the caudate nucleus—the cells of area 4 to the putamen and the cells of area 6 to the putamen and the external segment of the globus pallidus. The internal segment of the globus pallidus seems to be independent of the cortex and connects with Goll's and Burdach's nuclei.

The chapters on pathologic anatomy are the least satisfactory. They fail to describe any disease entity, as is clearly exposed in the discussion. Many regions of the central nervous system in which pronounced and characteristic lesions have been described were neither examined nor even mentioned, and the etiologic question is only touched on, in so vague a term as abiotrophy. On the other hand, the long-abandoned method of attempting to localize clinical signs, such as tremor or rigidity, in damaged areas of the brain has again been resumed, and, what is more, on statistically too small a number of cases. As a result Davison concludes from his material that disease of the globus pallidus leads to the rigidity and disease of the substantia nigra to tremor, while Alexander expresses the belief that tremor is caused by destruction of the medial marginal part of the putamen. A third author holds disease of the inferior olive responsible for tremor; a fourth states the substantia nigra is the only region rightfully involved in rigidity. L. Alexander contributes interesting details to the histology of status marmoratus.

The remarkable cinematographic demonstration of S. P. Goodhart and his able attempt to categorize the various types of extrapyramidal disease could have been greatly enhanced by a few characteristic illustrations.

P. F. A. Hoefer interprets action potentials of muscles in terms of impulses of the central nervous system appearing in and out of phase, activating and managing the motor unit "pools" under various conditions.

In a number of chapters the various pharmacologic, reeducational and surgical methods of treating paralysis agitans, chorea and athetosis are discussed.

P. C. Bucy reports 8 carefully selected cases of unilateral tremor or choreoathetosis in which great benefit was derived from resection of areas 4 and 6, and R. Meyers, 8 cases of paralysis agitans in which operation on the basal ganglia gave promising results.

R. Klemme, in five pages, not accompanied by any illustration or description of his method of premotor excision, reports that 39 of his patients with dystonia were "completely relieved and rehabilitated, without any clinical signs or symptoms."

In the last paper of the 700 page volume, T. J. Putnam discusses the remarkable effects of anterior chordotomy on *athétose double* and of bisection of the lateral pyramidal tracts of Parkinson tremor—an operation which, interestingly enough, does not result in paralysis. Nobody interested in any angle of the problems of the basal ganglia and the extrapyramidal system should miss this very informative book.

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